Archives of Dermatology and Syphilology

VOLUME 40 JULY 1939 NUMBER 1

COPYRIGHT, 1939, BY THE AMERICAN MEDICAL ASSOCIATION

TREATMENT-RESISTANT SYPHILIS

AN EVALUATION OF THE CAUSATIVE FACTORS IN EIGHTEEN CASES

WALTER BECKH, M.D.
AND
GEORGE V. KULCHAR, M.D.
SAN FRANCISCO

During the past decade the problem of treatment-resistant syphilis has received considerable attention in the German and French literature. One gains the impression that resistance to treatment, at least in these countries, is observed with increasing frequency. American reports, however, are few and have dealt with single or at the most a small number of cases. By far the largest series is that of Moore and Robinson,[1] who found 12 cases among the admissions to a large syphilis clinic during fifteen years. They concluded that treatment resistance was not increasing in frequency and was still a rare occurrence in this country. During the past six years, however, we have encountered 18 instances of treatment resistance in patients with early syphilis. It is the purpose of the present report to review these cases and to investigate the causative factors.

A thorough review of the literature has been made recently by Beerman.[2] The numerous causative factors suggested may be grouped as involving the host, the drug or the spirochete. At present the consensus, according to Beerman, seems to be that the host is the most important factor in treatment resistance.

The concept of treatment-resistant syphilis has been variously defined. The fixed positive Wassermann reaction of the blood and the occurrence of serologic relapses during therapy are regarded by some as manifestations of treatment-refractory syphilis. While this may in a

From the Division of Dermatology and Syphilology of the Stanford University School of Medicine.

1. Moore, J. E., and Robinson, H. M.: The Question of Arsphenamine-Resistant Syphilis, Arch. Dermat. & Syph. **21**:32 (Jan.) 1930.

2. Beerman, H.: The Problem of Treatment-Resistant Syphilis, with Special Reference to Arsphenamine-Resistant Syphilis: Review of the Literature and Experimental Study, Am. J. Syph., Gonor. & Ven. Dis. **20**:165 (March); 296 (May) 1936.

broad sense be regarded as treatment resistance, the concept is limited usually to patients presenting demonstrable lesions. Basically, the criteria for the diagnosis are (1) persistence of the initial lesions despite adequate therapy ("primary treatment resistance") or recurrences appearing during treatment ("secondary treatment resistance") and (2) persistence of Spirochaeta pallida in the lesions despite adequate treatment. The value of the basic criteria, particularly the presence of Spirochaeta pallida, cannot be denied. However, as both Gougerot and his co-workers [3] and Beerman have emphasized, the diagnosis frequently must be made from the appearance and course of the lesions. This is especially true of the late secondary recurrences, in which spirochetes often cannot be demonstrated. A positive Wassermann reaction of the blood, particularly when there has previously been a negative response, may be of assistance in confirming the clinical diagnosis.

During the six years ending June 1, 1937, among the 694 patients with primary and secondary syphilis admitted to the syphilis clinic of the Stanford University School of Medicine, 15 (2.2 per cent) manifested treatment resistance. Three additional patients observed elsewhere are included in this study, making a total of 18. In all the treatment resistance occurred during therapy. Relapses appearing after the cessation of treatment, even though adequate according to the usual standards, have been excluded. Fourteen of the patients were men, and 4 were women. All were white, as other races represent a small minority of the syphilitic population in this region. The ages varied from 20 to 64 years, 15 patients being less than 40. The clinical data are summarized in table 1.

The state of nutrition was fair or good in all patients. In none was the syphilitic infection complicated by other disease or pregnancy. There was no unusual history of past illnesses. Three of the 10 patients on whom data are available used alcohol in large amounts. The duration of observation varied from eleven to seventy-three months, the average being thirty-two and three-tenths months. After the appearance of treatment resistance the patients were followed for from three to forty-seven months, or an average of nineteen and four-tenths months.

Neoarsphenamine was used for 14, mapharsen for 3 and bismarsen for 1. All except one received heavy metal therapy either simultaneously or in alternation with the arsenic medication. Fifteen received either iodobismitol with saligenin or bismuth subsalicylate intramuscularly. One patient was given mercury rubs and another sobisminol (sodium bismuthate soluble) orally. Preliminary studies have indicated that the latter preparation is effective in the treatment of early syphilis.

TABLE 1.—*Summary of Clinical Data*

3. Gougerot, H.; Burnier; Ragu, and Weill: Syphilis arséno-récidivantes: Fréquence de la forme papulo-squameuse et du Bordet-Wassermann négatif, Ann. d. mal. vén. **25**:321 (May) 1930.

TABLE 1.—*Summary of Clinical Data*

Case No.	Sex	Age	Initial Diagnosis	Treatment Before Relapse (Total Amount)	Arsenical Dose, Mg. per Kg. of Body Weight	Bismuth Dose, Mg. per Kg. of Body Weight	Duration of Treatment Prior to Appearance of Treatment-Resistant Lesions	Regularity of Treatment, %	Type of Treatment Resistance	Dark Field Examination	Wassermann Test of Blood
1	F	27	Seropositive secondary	Neoarsphenamine and bismuth combined	Weight not recorded		.....	100	Primary	No data	Moderately positive
2	M	30	Seronegative primary	Neoarsphenamine and mercury rubs combined	Weight not recorded		.....	85	Primary	Positive	Strongly positive
3	M	32	Seropositive primary	Neoarsphenamine and bismuth combined	7.0	0.19	.....	100	Primary	Positive	Negative
4	M	27	Seropositive primary	Mapharsen and bismuth alternating	1.0	0.20	21 weeks*	100	Primary-secondary	Positive	No data
5	M	24	Seropositive primary	Mapharsen and bismuth combined	0.6	0.17	14 weeks*	79	Primary-secondary	Positive	Strongly positive
6	F	43	Seronegative primary	Neoarsphenamine, 11.2 Gm.	10.0	0	47 weeks	53	Secondary	No data	Strongly positive
7	M	39	Seronegative primary	Neoarsphenamine, 17.7 Gm.; bismuth, 6.48 Gm. combined	6.0	0.16	61 weeks	97	Secondary	No data	Strongly positive
8	M	26	Seronegative primary	Neoarsphenamine, 12.2 Gm.; sobisminol (oral) 98 Gm. combined	6.0	14.0	40 weeks	85	Secondary	Positive	Strongly positive
9	M	40	Seropositive primary	Neoarsphenamine and bismuth 5 years irregularly, then neoarsphenamine, 4.5 Gm., and bismuth, 13.2 Gm., alternating	No data	No data	6 years	...	Secondary	No data	Moderately positive
10	M	24	Seropositive secondary	Neoarsphenamine, 6.7 Gm.; bismuth, 2.4 Gm. combined	6.0	0.17	20 weeks	100	Secondary	Positive	Moderately positive
11	M	38	Seropositive secondary	Neoarsphenamine, 22.1 Gm.; bismuth, 6.7 Gm. combined	9.0	0.20	123 weeks	70	Secondary	Positive	Strongly positive
12	M	31	Seropositive secondary	Neoarsphenamine, 19.2 Gm.; bismuth, 6.5 Gm. combined	7.0	0.18	74 weeks	85	Secondary	Negative	Moderately positive
13	M	22	Seropositive secondary	Neoarsphenamine, 22.3 Gm.; bismuth, 9.6 Gm. combined	10.0	0.18	68 weeks	87	Secondary	No data	Moderately positive
14	M	37	Seropositive secondary	Neoarsphenamine, 4.2 Gm.; bismuth, 0.84 Gm. combined	8.0	0.13	7 weeks	100	Secondary	No data	No data
15	M	55	Seropositive secondary	Mapharsen, 0.72 Gm.; bismuth, 2.4 Gm. combined	0.8	0.15	21 weeks	86	Secondary	No data	Strongly positive
16	F	26	Seropositive secondary	Neoarsphenamine and bismuth alternating	No data	No data	5 years	Irregular	Secondary	No data	Strongly positive
17	M	64	Seropositive secondary	Bismarsen, 4 Gm.; bismuth, 10.5 Gm.	0.3	0.16	107 weeks	100	Secondary	No data	Strongly positive
18	F	24	Latent seropositive (treated)	Neoarsphenamine, 9 Gm.; bismuth, 3 Gm. combined	9.0	0.24	25 weeks	100	Secondary	No data	Moderately positive

* Duration of treatment prior to appearance of "secondary treatment resistance."

The arsenical was given in a weekly dose of either 0.45 or 0.6 Gm. of neoarsphenamine or 0.06 Gm. of mapharsen. The dose of bismarsen was 0.2 Gm. once a week. For the bismuth therapy the dose was 2 cc. (0.12 Gm.) of iodobismitol with saligenin and 1 cc. (0.13 Gm.) of bismuth subsalicylate. The 1 patient receiving sobisminol orally was given 1.2 Gm. daily. The dose of both the arsenical and the heavy metal was calculated on the basis of milligrams per kilogram of body weight, as shown in table 1.

Either the "alternating" or the "combined" system of treatment was ordinarily used. With the former, courses of ten weekly injections of an arsphenamine were alternated with courses of twenty weekly injections of a heavy metal preparation, except that during the first ten weeks both were given simultaneously. In the "combined" system (simultaneous, concurrent, continuous) the arsphenamine and the heavy metal

TABLE 2.—*Frequency of Occurrence of the Clinical Manifestations of Treatment Resistance in Eighteen Patients*

Type of Lesion	Number of Patients
Persistence of chancre	1
Chancriform recurrence	1
Generalized maculopapular syphilids	2
Papular and eczematoid syphilids of genitalia	7
Papulosquamous psoriasiform syphilids	10
Frambesiform and pustular syphilids	1
Annulopapular and circinate syphilids	3
Grouped follicular syphilids	1
Split papules	1
Anal condylomas	1
Secondary syphilids of mouth and larynx	7
Nodulоulcerative late syphilids	2
Periostitis	1

were given simultaneously once a week for twenty weeks, and the arsphenamine was then omitted for five weeks, after which a second course of twenty injections was given. The initial course of heavy metal was continued for thirty doses, and a second course of forty injections was given after an interval of five weeks. Of the 2 patients treated otherwise, 1 received alternating courses of bismarsen and iodobismitol with saligenin, and the other was given only neoarsphenamine. The regularity of treatment shown in table 1 represents the percentage of the total number of appointments for treatment which were kept.

Treatment resistance is classified in table 1 as (1) primary, when the original lesions (chancre or secondary) failed to respond to routine therapy; (2) primary-secondary, when the initial lesions were treatment resistant but eventually involuted, and later there were refractory recurrences during treatment; (3) secondary, when the original lesions responded normally but a treatment-resistant relapse occurred subsequently during therapy.

The clinical manifestations of treatment resistance were variable, and for the most part involved the skin and mucous membranes. They are listed in table 2 according to the frequency of their occurrence.

The lesions were for the most part similar to those usually seen in early syphilis. The psoriasiform type occurred most commonly either in the form of the usual papulosquamous syphilid or as atypical eczematoid or psoriasiform plaques. From the morphologic characteristics of the latter, as Jessner [4] and Gougerot and his associates [3] have pointed out, the diagnosis of treatment-refractory syphilis may be made. Usually the eruption was not profuse, and often it was confined to the face or extremities. Occasionally the lesions were limited to the palms and soles. The lesions were infiltrated plaques, brownish red or deeply erythematous. At times it was difficult to differentiate the eruption from psoriasis. The serpiginous arrangement and precocious secundotertiary character of the lesions, as well as the color and absence of typical imbricated scaling, aided in the differential diagnosis. The demonstration of Spirochaeta pallida on dark field examination confirmed the clinical diagnosis in 4 of the 5 cases in which a search was made. When the clinical differentiation could not be made with certainty, a concomitant serologic relapse or the persistence of a positive Wassermann reaction of the blood was of assistance. Finally, in some, the response to measures directed toward overcoming the resistant state confirmed the clinical diagnosis.

Three of the 18 patients (nos. 1, 2 and 3 in table 1) were refractory to treatment from the beginning (primary treatment resistance). In 2 (nos. 4 and 5) the initial lesions were resistant to treatment but eventually involuted, only to be followed by refractory recurrences (primary-secondary treatment resistance). In the remaining 13 patients the original lesions responded normally to treatment, the clinical manifestations of resistance appearing subsequently (secondary treatment resistance). In collating the anamnestic data, we have considered the three types together.

The duration of treatment prior to the occurrence of refractory lesions, the primarily resistant patients being omitted, varied from seven to one hundred and twenty-three weeks, the average being thirty-two and eight-tenths weeks. The manifestations of treatment resistance appeared within the first twenty-five weeks of therapy in 6 of the 13 patients with the secondary type of treatment resistance on whom data are available.

Treatment resistance first appeared during the simultaneous phase in all the 13 patients who received combined therapy. Among the 3

4. Jessner, M.: Ueber salvarsanresistente Lues, Med. Klin. **19**:857 (June) 1923.

patients receiving the alternating type of treatment, resistance occurred first during arsphenamine medication in 1; for the other 2, data as to the phase of treatment are not available. All, however, were subsequently refractory to both arsphenamine and bismuth medication. In the single patient who received neoarsphenamine only, heavy metal therapy was not used during the resistant state. One patient showed resistant lesions while receiving bismarsen and failed to respond to

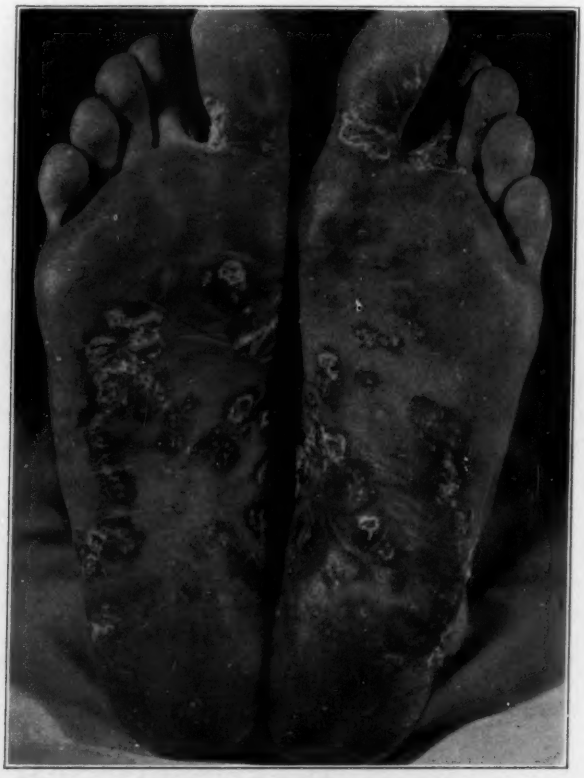


Fig. 1 (case 5).—Psoriasiform treatment-resistant syphilids on the soles, occurring after forty-five weeks of "combined" therapy. Spirochaeta pallida was demonstrated by dark field examination.

subsequent injections of iodobismitol with saligenin. It appears that among the patients of the present series at least, specific drug fastness is not an important factor in treatment resistance.

The serologic reactions in treatment-resistant syphilis are variously reported. While negative Wassermann reactions are reputedly common, seronegativity was encountered but once (case 3) among the patients in the present series. The reaction in this case subsequently became positive with the persistence of the refractory state. The 3

patients with primary treatment-resistant syphilis showed a persistently positive Wassermann reaction of the blood. Among the 11 patients with the secondary type of treatment resistance on whom data are available, the Wassermann reaction prior to the appearance of treatment resistance was negative for 3, fluctuated between negative and positive for 1, and was persistently positive for 7. A change in the serologic reaction from negative to positive occurred simultaneously with the development of treatment-resistant lesions in the 3 cases in which the

Fig. 2 (case 3).—Psoriasiform treatment-resistant lesions persisting after seventy-two weeks of "combined" therapy. Spirochaeta pallida was demonstrated by dark field examination.

Wassermann reaction had been previously negative. The high incidence of positive serologic reactions is in accordance with the observations of Gougerot and his associates but contrary to those of Hudélo and Rabut,[5] Aristoff [6] and others, who have reported negative Wassermann

5. Hudélo and Rabut: Syphilis secondaire, avec sérologie négative, Bull. Soc. franç. de dermat. et syph. **34**:195 (April) 1927.

6. Aristoff, G., cited by Beerman.[2]

reactions to be frequent in treatment-resistant syphilis. Variations in the sensitivity of serologic tests may in part account for the conflicting reports.

Examinations of the cerebrospinal fluid either during or soon after the development of the resistant state were made in 12 cases. In 11 the cerebrospinal fluid was normal, while in 1 an increase in cells and protein, a partially positive Wassermann reaction and an abnormal colloidal gold curve were found. The cerebrospinal fluid in 2 was negative before the appearance of treatment resistance and was not reexamined. None of the patients presented clinical evidence of visceral or neurosyphilis.

Conjugal treatment resistance has been cited as evidence for a treatment-refractory strain of Spirochaeta pallida. In 4 of the 18 cases

TABLE 3.—*Effects of Various Methods of Therapy in Treatment-Resistant Syphilis*

Case No.	Continuance of Previous Treatment	Change of Drug	Intensification of Treatment	Fever Therapy
1	Effective	.....	.....	.....
2	.....	Effective	.....	.....
3	Ineffective	Ineffective	Ineffective	Ineffective
4	Ineffective	.....	Effective	.....
5	.....	Ineffective	Ineffective	Effective
6	Ineffective	Effective	.....	.....
7	.....	Effective	.....	.....
8	.....	.....	Effective	.....
9	.....	Effective	.....	.....
10	.....	Ineffective	Ineffective	Effective
11	.....	.....	Effective	.....
12	.....	Effective	.....	.....
13	.....	.....	Effective	.....
14	Ineffective	Effective	.....	Ineffective (short course)
15	.....	Effective	.....	.....
16	Ineffective	Effective	.....	.....
17	.....	Effective	.....	.....
18	Ineffective	Effective	.....	.....

the infected sexual partner could be examined and followed. The response to treatment of all 4 was normal, and no evidence of the transmission of a treatment-resistant strain could be found.

According to Jessner, patients with treatment-resistant syphilis are frequently intolerant of the arsphenamines. It has been suggested that treatment-resistant persons metabolize arsphenamine in a different manner, so that the therapeutic efficiency of the drug is impaired. Seven of the 18 patients had various types of treatment reactions. These included mild arsphenamine dermatitis for 2, peripheral neuritis for 1, a nitritoid reaction for 2, gastrointestinal disturbances for 2, and a febrile reaction following bismarsen for 1. On the whole, reactions appeared to be more frequent than might be expected.

The effectiveness of various measures used in the treatment of resistant syphilis is given in table 3. Continuance of the treatment used before the clinical appearance of the refractory state proved successful

in only 1 of the 7 cases in which this measure was tried. On the other hand, a change of drug (either of the arsphenamine or heavy metal) was effective in 10 of 13 cases. Intensification of treatment, either through increase in the frequency of administration or by a combination of drugs, was effective in 4 of 7 cases. Fever therapy was successful in 2 of 4 cases, although in 1 in which this measure was ineffective only five injections of typhoid vaccine were given. The treatment-resistant lesions persisted despite a trial of the various arsphenamines, mercury and bismuth preparations, typhoid vaccine and liver extracts parenterally in 1 case (case 3). From these results it would seem that a change of drug is the most effective treatment for refractory syphilis, but as this measure was used with greater frequency than others, no direct comparison can be made. Similarly, since the number of patients given fever therapy was small and the measure was reserved for those who were refractory to other types of treatment, its relative effectiveness cannot be fully evaluated. Our results, however, do suggest, in accord with the experience of others, that continuation of the treatment used before the clinical appearance of resistance is a relatively ineffectual measure.

The numerous factors concerned in treatment resistance have been summarized by Beerman. These may be grouped as involving the host, the spirochete or the drug, either singly or through an interaction of two or more factors. The most commonly cited host factors are malnutrition, poor health, endocrine disturbances, hepatic insufficiency, failure of the cellular mechanism of the body (blood, lymphoid or reticuloendothelial system) and faulty drug metabolism and intolerance to treatment. The explanations advanced for the role of the host, however, are largely conjectural and lack experimental confirmation. The age, race and sex distribution did not differ significantly from the clinic average. The general health and state of nutrition were good in all. There was no evident hepatic disease or endocrine disturbance. Reactions to treatment, however, were more frequent than expected. Regularity of treatment did not appear to be a factor in treatment resistance, since only 3 of the 17 patients on whom data are available kept less than 80 per cent of their regularly scheduled appointments for treatment.

No evidence to support the concept of a primary treatment-refractory strain of Spirochaeta pallida could be found. The response to treatment was normal in the 4 conjugally infected partners. This is in general accord with the experience of other workers and substantiates the impression that factors other than the strain of spirochete are primarily concerned in treatment resistance. Attempts to perpetuate the treatment-refractory characteristics in the experimental animal have been uniformly unsuccessful, with the exception of the case reported by Beerman, in which partial refractoriness could be preserved in serial animal passage.

Treatment resistance also has been attributed to changes in the quality of the arsphenamines. Stokes [7] and others [8] have suggested that attempts to decrease the toxicity of the arsphenamines may result in therapeutically less effective preparations. Langer [9] and Zoon,[10] however, have concluded that the therapeutic efficacy of the arsphenamines has not been impaired, since the same drugs have been used for successfully treated patients and for resistant ones. Silberstein [11] found from comparative studies that the therapeutic effectiveness of the arsphenamines had not changed. The difference in the therapeutic effectiveness may in a large part be due to differences in dosage and methods of administration of the arsphenamines. Therapeutically ineffective drugs can be eliminated as a cause in the cases reported here, as various types and brands of the arsphenamines were used. Similarly, during the six year period in which the cases of treatment-refractory disease occurred, many patients were treated effectively with the same preparations.

In practice, wide variations exist in the length of the course and the dose of the arsphenamines. For neoarsphenamine the recommended dose is from 9 to 13 mg. per kilogram (Stokes), while that for mapharsen is 0.9 mg. per kilogram of body weight. For 7 of the 11 patients treated with neoarsphenamine on whom there are available data (table 1) the amount received was less than the therapeutic minimum when calculated according to body weight. For 2 of the 3 patients who received mapharsen the dose per kilogram of body weight was less than the prescribed minimum. For 9 of the 14 patients, therefore, the dose of arsphenamine was inadequate on the basis of weight. The amount of bismuth per kilogram of body weight was within the recommended range for all patients.

The relation between the frequency of treatment resistance and the system of therapy was determined. Thirteen of the 18 patients received "combined" therapy. Nine received a dose of the arsphenamine less than the minimum. In addition, 1 patient was treated with bismarsen, which in effect is combined therapy, and another received only con-

7. Stokes, J. H.: Modern Clinical Syphilology, Philadelphia, W. B. Saunders Company, 1934, pp. 193 and 330.

8. Nicolas, J.; Massia, G., and Lacassagne, J.: Sur la fréquence croissante des syphilis arséno-resistantes dans la région lyonnaise, Bull. Soc. franç. de dermat. et syph. **35**:132 (Feb.) 1928. Lacassagne, J., and Lebeuf, F.: Comment expliquer l'arséno-resistance, J. méd. franç. **20**:272 (Aug.) 1931.

9. Langer, E.: Ueber therapieresistente Lues, Med. Klin. **20**:1171 (Aug.) 1924; Therapieresistente Lues, Therap. d. Gegenw. **71**:118 (March) 1930.

10. Zoon, J. J.: Ueber gegen Neosalvarsan resistente Syphilis, Dermat. Ztschr. **63**:327 (April) 1932.

11. Silberstein, S.: Zur Frage der salvarsanresistenten Lues, Arch. f. Dermat.. & Syph. **147**:116 (April) 1924.

tinuous injections of neoarsphenamine. The remaining 3 patients received the "alternating" form of treatment. The dose of arsphenamine for the single patient on whom data are available was adequate for the body weight. It is significant that treatment resistance occurred with much greater frequency in patients receiving the "combined" type of therapy, although alternating treatment was used in a considerably greater number of patients during the same period. The ineffectiveness of the "combined" system of therapy in preventing relapse has been reported by Beckh and Barnett.[12] All the clinical relapses during combined therapy in this series were treatment refractory, while resistant relapses were not encountered among patients receiving the alternating form of treatment.

The extensive clinical experience of the Cooperative Clinical Group [13] has recently confirmed the opinion that the small dose scale may be an important factor in the induction of treatment resistance. On the experimental side, the effect of prolonged underdosage on the production of drug fastness has been established (Launoy and Levaditi,[14] Akatsu and Noguchi,[15] Brown and Pearce,[16] Feldt [17] and others). The long courses of the arsphenamines usually in doses inadequate for the body weight, as carried out in the "combined" system of treatment, may produce a similar result. Owing to the short interval between courses, both the arsphenamine and the heavy metal are received almost continuously. From the clinical and experimental data it seems likely that the more frequent occurrence of treatment resistance among the patients given "combined" therapy is due, at least in part, to prolonged underdosage with the arsphenamines.

---

12. Beckh, W., and Barnett, C. W.: Comparative Effects on Early Syphilis of Combined and of Alternating Treatment, Arch. Int. Med. **63**:974 (May) 1939.

13. Clark, T.; Parran, T., Jr.; Cole, H. N.; Moore, J. E.; O'Leary, P. A.; Stokes, J. H., and Wile, U. J.: Cooperative Clinical Studies in the Treatment of Syphilis: Introduction, Ven. Dis. Inform. **13**:135 (April 20) 1932. Stokes, J. H.; Cole, H. N.; Moore, J. E.; O'Leary, P. A.; Wile, U. J.; Clark, T.; Parran, T., Jr., and Usilton, L. J.: Cooperative Clinical Studies in the Treatment of Syphilis: Early Syphilis, ibid. **13**:165 (May 20); 207 (June 20); 253 (July 20) 1932.

14. Launoy, L., and Levaditi, C.: Création d'une râce de Treponema pallidum résistante au mercure, Compt. rend. Soc. de biol. **72**:653 (April) 1912.

15. Akatsu, S., and Noguchi, H.: The Drug Fastness of Spirochetes to Arsenic, Mercurial, and Iodide Compounds in Vitro, J. Exper. Med. **25**:349 (March) 1917.

16. Brown, W. H., and Pearce, L.: Superinfection in Experimental Syphilis Following the Administration of Subcurative Doses of Arsphenamine and Neoarsphenamine, J. Exper. Med. **33**:553 (May) 1921.

17. Feldt, A.: Ueber Arzneifestigung von Spirochäten im Tierversuch, Klin. Wchnschr. **11**:1378 (Aug. 13) 1932.

However, the absence of treatment resistance in many patients treated by this scheme of therapy, as well as the occasional occurrence of treatment refractoriness with other systems of treatment, suggests that some as yet undefined intrinsic host factor may also play a part. It does not seem unlikely that treatment resistance is frequently the result of interaction of underdosage and "host factors."

SUMMARY

1. Eighteen cases of treatment-resistant syphilis encountered over a six year period are reported.

2. The criteria for the diagnosis are discussed, and a description of the clinical manifestations is given.

3. Little evidence could be found that specific host factors are primarily concerned in the production of treatment resistance. Likewise, treatment refractoriness could not be ascribed to infection with a treatment-resistant strain of Spirochaeta pallida.

4. Treatment resistance was observed to occur with much greater frequency in patients treated by the "combined" (simultaneous, concurrent, continuous) system of therapy than in patients receiving the "alternating" type of treatment. It is suggested that the high incidence of treatment resistance observed among patients receiving the "combined" type of therapy is due to prolonged underdosage with the arsphenamines.

5. In the management of the treatment-refractory patient, continuance of the same treatment is relatively ineffective. Intensification of treatment or change of drug or both is more frequently successful. In patients refractory to these measures fever therapy is often effective.

LICHENOID AMYLOIDOSIS

REPORT OF TWO CASES FEATURING ABSENCE OF CUTANEOUS LESIONS OVER SOME OF THE CRURAL TRIBUTARIES OF THE INTERNAL SAPHENOUS VEINS

E. WILLIAM ABRAMOWITZ, M.D.
AND
LUDWIG ISAAK, M.D.
NEW YORK

We recently encountered a case of classic localized cutaneous lichenoid amyloidosis of the legs in which papules were absent over some of the superficial crural veins. One of us (L. I.) had observed a case of similar involvement abroad. This unusual distribution of the lesions has not been mentioned in other cases of localized cutaneous amyloidosis cited in the literature and is the subject of this report.

REPORT OF CASES

CASE 1.—Mr. J. O. appeared at the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital on Aug. 29, 1938. He was 62 years of age, of Austrian birth, married and a cigar maker. His habits were regular, and except for occasional constipation he had always been in good health. He had undergone hemorrhoidectomy twenty-eight years before, and about ten years before had begun to complain of itching of the legs, which was soon followed by an eruption in this area, especially on the shins.

When he was first observed, a profuse eruption of pinhead-sized papules involved the entire circumference of the legs. The papules were closely aggregated, each one being distinct and flat topped and a waxy yellowish brown. They were firm to the touch and yet appeared semitransparent, as if they contained fluid. Long linear marks were present, the result of scratching. Over the middle of the anterior crest of the left tibia it was noted that the papular lesions were not present over one of the superficial crural veins.

An intracutaneous injection of 0.1 cc. of a 1 per cent solution of congo red in the affected area of the left tibia was followed in about twenty-four hours by a distinct rose red coloration of all the papular lesions in this location, the unaffected skin remaining normal in color. This red discoloration remained for almost one month. A subcutaneous injection was then made, with similar results.

From the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital, Columbia University.

A biopsy specimen was taken from one of the lesions on the left leg.

Histologic Examination (Dr. D. L. Satenstein).—The amyloid degeneration extended from the under surface of the epidermis to the upper cutis to about the level of the lower margin of the surrounding epidermis. This area was sharply

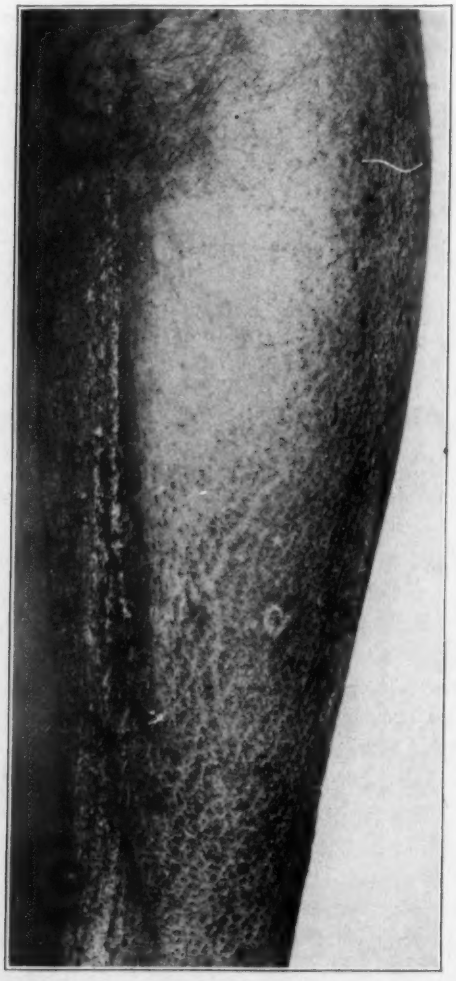


Fig. 1 (case 1).—Anterior surface of the left leg, showing profuse lichenoid papules. The lesions are absent over one of the superficial veins over the middle of the crest of the tibia. The lines on the inner side of the leg are due to scratching.

differentiated from the surrounding framework of the cutis. Between the basal zone of the epidermis and this area there was a narrow strip of unaffected cutis. With the routine hematoxylin and eosin stain the differentiated area was noted

to take on a lilac tone, in contrast to the pinkish eosin tone of the unaffected tissue. With the methyl violet stain this area assumed a brilliant red color. The area was not completely homogeneous, as some parts stained less with the methyl violet. The collagen bundles in this area were swollen, somewhat homogeneous and in part structureless. The cellular elements in this area were apparently unaffected. No elastic tissue fibers were demonstrable in the pathologic zone, whereas in the surrounding zones the elastica was normal. The overlying epidermis was flattened; the rete pegs and the papillary bodies were completely effaced.

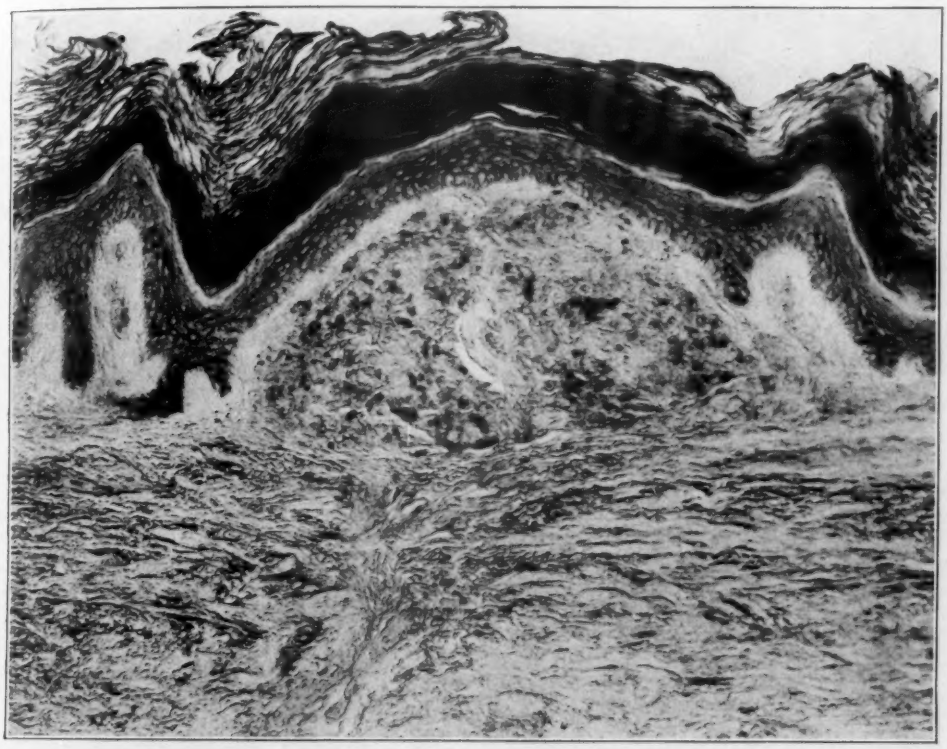


Fig. 2 (case 1).—Photomicrograph (× 115) of a section fixed in Bouin's solution and stained with methyl violet. It shows the flattened epidermis with overlying hyperkeratosis. The amyloid nodules in the upper papillary portion of the cutis are sharply differentiated from the surrounding part of the cutis.

The patient underwent a complete physical examination by the department of internal medicine, and nothing essentially abnormal was found. The excretion of congo red after intravenous injection was normal. Examination of the urine gave negative results, and the Wassermann reaction was negative. The blood count was within the normal range.

The clinical appearance, the local congo red test [1] and the histologic report confirmed the diagnosis of localized amyloidosis of the skin. The patient received

1. Nomland, R.: Localized (Lichen) Amyloidosis of the Skin, Arch. Dermat. & Syph. **33**:85 (Jan.) 1936.

weekly fractional (75 roentgen) doses of unfiltered roentgen radiation. After eight treatments the itching was almost entirely gone, all the raised papular lesions had flattened, appearing as brownish pigmented spots. However, a pink discoloration was still noted after an intradermal injection of congo red.

CASE 2.—One of us (L. I.) presented a man aged 53 for diagnosis before the dermatologic society of Frankfort on the Main, Germany, on Sept. 26, 1929.[2] The patient had been complaining for ten years of severe itching of the legs,

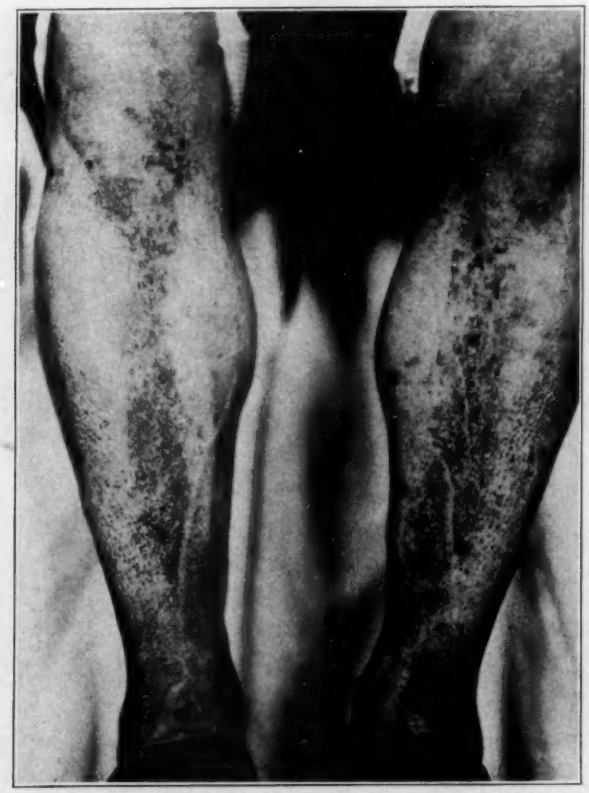


Fig. 3 (case 2).—Distribution of papular lesions; these were absent along the course of some of the superficial veins in the tibial regions.

followed by the appearance about one year before presentation of yellow papules varying in size from that of a pinhead to that of a lentil. The eruption was located only on the legs, particularly on the shins. Gutmann[3] suggested the possibility of local amyloidosis of the skin. It was noted at this time that the skin over the course of some of the superficial veins of the shins was free of any lesions.

2. Isaak, L.: Zentralbl. f. Haut- u. Geschlechtskr. **33**:534, 1930.
3. Gutmann, in discussion on Isaak.[2]

This patient was presented again at the next meeting, on Oct. 31, 1929.[4] A biopsy specimen had been taken, and the presence of amyloid was accepted as definitely demonstrated by several pathologists (metachromasia was seen with gentian violet, a light yellowish coloration after Van Gieson's stain and definite redness with methyl violet; other stains, not mentioned, gave negative results). No cutaneous tests with congo red were performed.

Biopsy material removed in this case was submitted by one of us (L. I.), to Dr. D. L. Satenstein, who reported an almost exact resemblance of the histologic appearance to that in case 1.

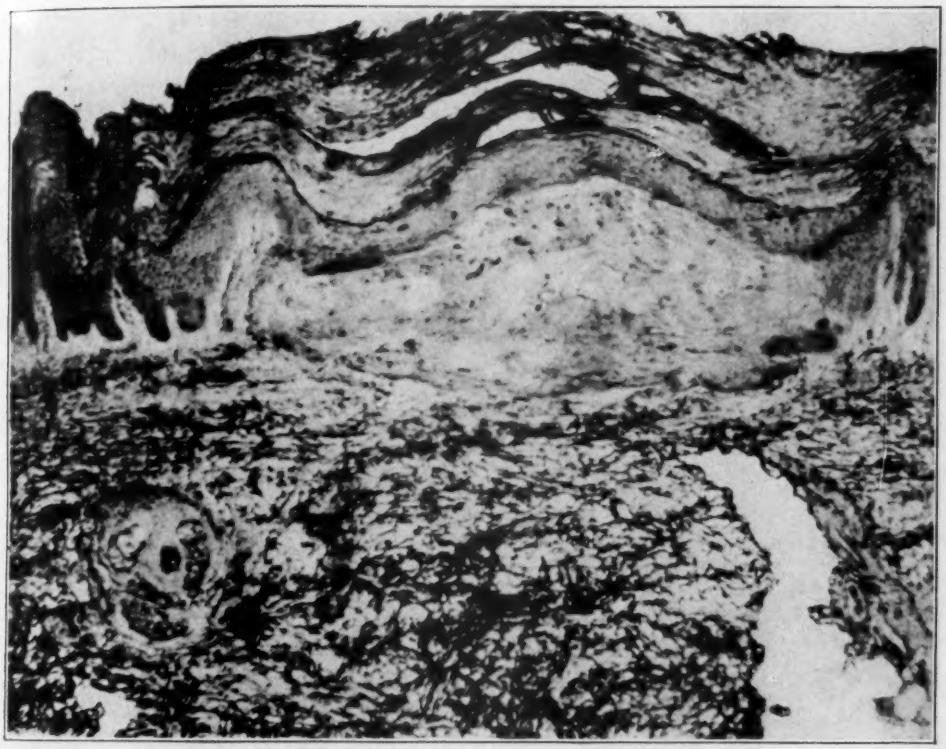


Fig. 4 (case 2).—Photomicrograph (× 115) of a cutaneous lesion, showing similar histologic appearance to that in case 1 (fig. 2).

This case may be accepted also as one of localized amyloidosis of the skin of the legs.

COMMENT

The significance of the absence of lesions over the course of some of the superficial veins may or may not be of importance. No attempt is made to explain this peculiarity.

4. Isaak, L.: Zentralbl. f. Haut- u. Geschlechtskr. **33**:535, 1930.

SUMMARY AND CONCLUSIONS

Two cases are reported of lichenoid amyloidosis of the legs with peculiar absence of lesions over the superficial crural veins.

One of these patients (case 1) was treated with fractional (75 r) doses of unfiltered roentgen radiation weekly, with relief from itching and considerable but not entire resolution of the lesions.

IODOCHOLEATE: A NEW FUNGICIDAL PREPARATION

PRELIMINARY REPORT

WALTER F. LEVER, M.D.

BOSTON

In the investigations which have been carried out to determine the bactericidal and fungicidal properties of the various antiseptics, iodine stands out as the most valuable one.

Nye [1] found that "an aqueous solution of iodine apparently possesses more of the desirable prerequisites for an antiseptic solution than any of the other solutions that were tested." Schamberg and his associates [2] stated that "iodine in metallic form appears to be the strongest fungicide."

However, iodine in the form of tincture of iodine or compound solution of iodine U. S. P. has several serious disadvantages; (1) It is caustic; (2) it combines to a great extent with the proteins of the skin and is thus rendered inert, and (3) its volatility is high and therefore its fungicidal action is exerted over a rather short period. Sharlit and Highman,[3] who expressed the belief that "iodine is the desirable fungicide," said: "A constant stream of iodine acting over a long period of time, reaching the skin in fungicidal strength yet not irritating the skin is a desideratum."

Lately, a new iodine compound has been discovered by Goedrich,[4] iodocholeate. Goedrich found that bile salt has a great affinity for iodine; even in the dry state this salt combines with iodine to form a dark crystalline compound, iodocholeate. A part of the iodine goes into chemical combination with the bile salt, is not titratable with sodium

---

From the Department of Dermatology and Syphilology, Massachusetts General Hospital, C. Guy Lane, M.D., Chief.

1. Nye, R. N.: The Relative in Vitro Activity of Certain Antiseptics in Aqueous Solution, J. A. M. A. **108**:280 (Jan. 23) 1937.

2. Schamberg, J. F.; Brown, H., and Harkins, M. J.: The Chemotherapy of Ringworm Infections: Preliminary Report, Arch. Dermat. & Syph. **24**:1033 (Dec.) 1931.

3. Sharlit, H., and Highman, W. J.: The Use of Tetraiodomethenamine in Flexible Collodion in the Treatment of Dermatophytosis, Arch. Dermat. & Syph. **16**:697 (Dec.) 1927.

4. Goedrich, P.: New Iodine-Bile Compound (Iodocholeate), J. Am. Pharm. A. **36**:509 (June) 1937.

thiosulfate and possesses no fungicidal properties. The other part of the iodine forms an adsorption compound with the bile salt, is titratable and is active as a fungicide. Iodocholeate gives stable solutions in alcohol or water or mixtures of the two. It has been found that an aqueous solution with an addition of 15 to 20 per cent alcohol is the most desirable form. This solution has the color of any iodine solution but is slightly more viscous because of the addition of bile. For therapeutic purposes a solution of 1 to 2.5 per cent is most suitable. Iodocholeate can be incorporated easily in ointments. An oxycholesterol-petrolatum base has proved to be satisfactory. The formula used for a 2.5 per cent ointment is:

Iodocholeate powder	11.7 Gm.
Oxycholesterol-petrolatum base	38.3 Gm.
Distilled water	10.0 cc.

The fact that in iodocholeate the iodine is adsorbed to bile salt explains the following differences between it and tincture of iodine, as first pointed out by Goedrich:

1. The iodine in iodocholeate is released from its adsorption to bile salts as free iodine more slowly than the iodine in the tincture—in other words, is less volatile.

2. The iodine in iodocholeate combines less with protein than the iodine of the tincture.

These two facts offer the explanation for the superiority of iodocholeate over tincture of iodine.

LABORATORY STUDIES

Iodocholeate Is Less Irritating to Living Tissue.—The reasons for this are: 1. The iodine in iodocholeate acts on the skin more gradually because of its slow liberation from the bile salts. 2. The iodine in iodocholeate causes less damage to the protein of the skin because of its weak affinity for proteins. The little-irritating action of iodocholeate is its greatest asset. Goedrich instilled drops of tincture of iodine and of iodocholeate of the same strength into the eyes of rabbits. The iodocholeate-treated eyes showed practically no irritation, while in those in which tincture of iodine was instilled severe corneal ulcerations developed. While tincture of iodine given to rabbits by means of a stomach tube led to severe ulcerative gastritis, iodocholeate did not affect the stomach wall.[4]

Patch tests were made on 50 patients with normal skin either on the inside of the upper part of the arm or on the inside of the thigh with tincture of iodine and iodocholeate of 1, 2.5 and 5 per cent concentrations. The tests were read after forty-eight hours. Redness at the site

of the patch test was called + and vesiculation ++. Table 1 shows that iodocholeate is less irritating to the skin. Particular stress may be placed on the fact that the 2.5 per cent iodocholeate ointment led to redness in only 8 per cent of the cases and no vesicular reaction, as compared with redness in 32 per cent and vesiculation in 6 per cent for tincture of iodine ointment. Even 5 per cent iodocholeate ointment caused no vesicular reactions, while 5 per cent tincture of iodine caused them in 38 per cent.

Iodocholeate Has Greater Fungicidal Power in the Presence of Organic Material than Tincture of Iodine.—The iodine in the tincture and in compound solution of iodine combines with organic matter to a great extent. This decreases its effectiveness. The iodine in iodocholeate, because of its adsorption to bile salt, combines to a much slighter degree; therefore it acquires greater fungicidal power on the skin, in the

TABLE 1.—*Patch Tests with 1, 2.5 and 5 per Cent Tincture of Iodine and Iodocholeate (Liquid and Ointment) Done on Fifty Patients*

Tincture of Iodine	Reactions, %			Iodocholeate	Reactions, %		
	—	+	++		—	+	++
Liquid				Liquid			
1%	78	20	2	1%	94	6	..
2.5%	14	60	26	2.5%	60	28	12
5%	..	36	64	5%	22	50	28
Ointment							
1%	88	12	..	1%	98	2	..
2.5%	62	32	6	2.5%	92	8	..
5%	14	48	38	5%	68	32	..

Minus sign indicates negative reaction; plus sign, redness; plus signs, vesiculation.

presence of serum or pus and on Sabouraud's medium, which contains organic material in the form of peptone and agar. A lower concentration of iodocholeate than of tincture of iodine is required in Sabouraud's medium to prevent the growth of fungi.

Various amounts of a 2.5 per cent solution of tincture of iodine or iodocholeate were added to Sabouraud's medium while it was still liquid, to obtain various concentrations. For example, to obtain a concentration of 0.125 per cent, 0.6 cc. of 2.5 per cent iodocholeate or tincture of iodine was mixed with 12 cc. of Sabouraud's medium. The mixtures were poured on Petri dishes, and then cultures of Microsporon lanosum, Trichophyton or Epidermophyton were planted.

It was found that the average concentrations necessary to prevent the growth of Microsporon were 0.25 per cent of tincture of iodine and 0.167 per cent iodocholeate; for the prevention of the growth of Epidermophyton, 0.125 per cent tincture of iodine and 0.042 per cent iodocholeate; for Trichophyton, 0.125 per cent tincture of iodine and

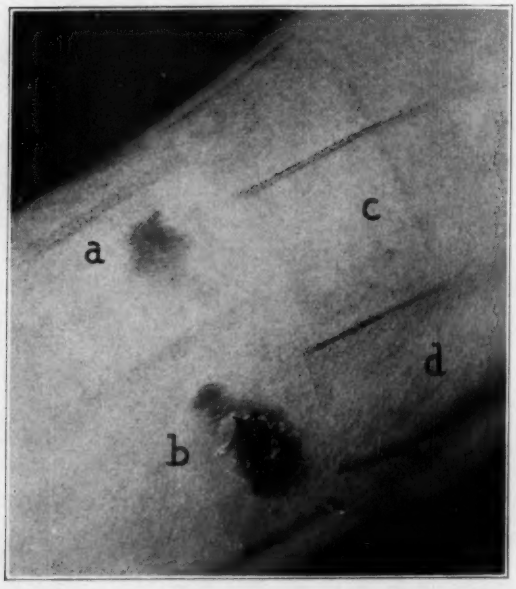


Fig. 1.—Patch tests on the arm: *a* with 2.5 and *b* with 5 per cent tincture of iodine ointment; *c* with 2.5 and *d* with 5 per cent iodocholeate ointment.

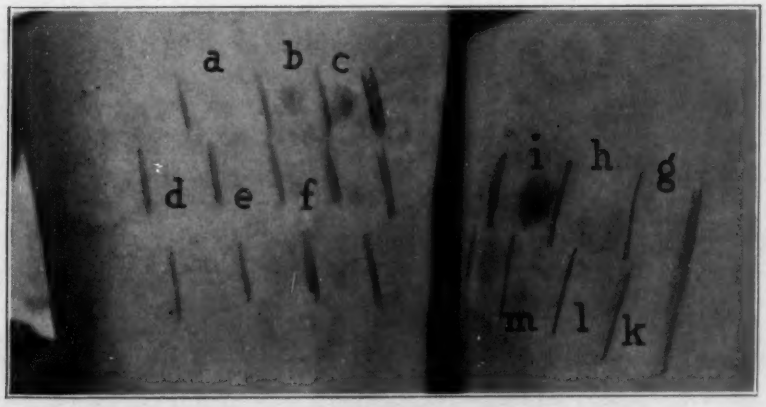


Fig. 2.—Patch tests on the thighs; *a* with 1, *b* with 2.5 and *c* with 5 per cent tincture of iodine solution; *d* with 1, *e* with 2.5 and *f* with 5 per cent iodocholeate solution; *g* with 1, *h* with 2.5 and *i* with 5 per cent tincture of iodine ointment; *k* with 1, *l* with 2.5 and *m* with 5 per cent iodocholeate ointment.

TABLE 2.—*Growth of Fungi (Microsporon lanosum, Epidermophyton, Trichophyton) on Sabouraud's Medium to Which Either Tincture of Iodine or Iodocholeate Was Added in Various Concentrations*

Fungus	Growth with Given Concentration of Fungicide								
	0.5 %	0.38 %	0.25 %	0.167 %	0.125 %	0.083 %	0.063 %	0.042 %	0.031 %
With Iodocholeate Used as Fungicide									
Microsporon	– – – – – 100%	– – – 100%	– – – – – – – – – – – 92%	– – – – – – – + + + 64%	– – – – + + + + + + + + 38%	+ + + + + + + + + 0%	+ + + + + 0%	+ + + 0%	+ 0%
Epidermophyton	..	..	– –	– – – –	– – – – – – – 100%	– – – – – – – – – + + 82%	– – – – – – – – + + + 73%	– – – – – – + 67%	– – – + + + 43%
Trichophyton	–	–	– – – – – 100%	– – – – – – – – – 100%	– – – – – – – – – – – + + 86%	– – – – – – – – – – + + + 77%	– – – + + + + + + + + 25%	– – + + + + + 29%	+ + + 0%
With Tincture of Iodine Used as Fungicide									
Microsporon	– – – – – 100%	– – + 67%	– – – – – – – – + + + + 67%	– – – – – + + + + + + 45%	+ + + + + + + + + + + + 0%	+ + + + + + + + + 0%	+ + + + + 0%	+ + + 0%	+ 0%
Epidermophyton	..	..	– –	– – – –	– – – – – – – – + + 80%	– – – – – + + + + + + 45%	– – + + + + + + + + + 18%	– + + + + + + + + 11%	– + + + + + + 14%
Trichophyton	–	–	– – – – + 100%	– – – – – – – + + 78%	– – – – – – – + + + + + + + 50%	– – – + + + + + + + + + + 23%	+ + + + + + + + + + + + 0%	+ + + + + + + 0%	+ + + 0%

Plus sign indicates growth; minus sign, no growth. The figures below the plus and minus signs indicate the percentage in which growth was prevented.

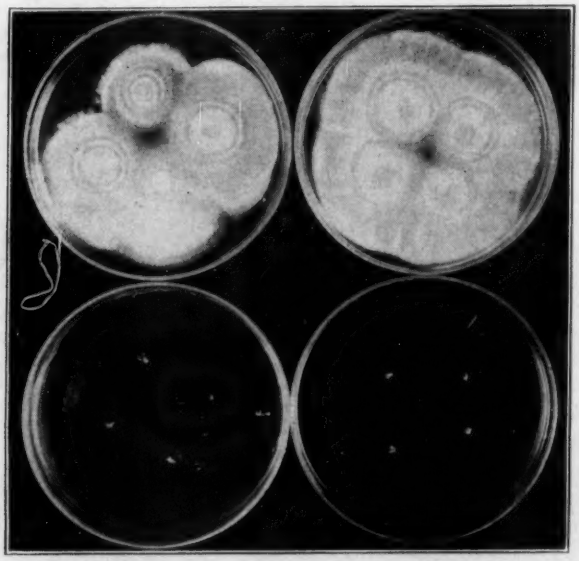


Fig. 3.—Cultures of Microsporon lanosum on Sabouraud's medium to which either tincture of iodine or iodocholeate was added. Upper row: left with 0.167 per cent and right with 0.125 per cent tincture of iodine; lower row: left with 0.167 per cent and right with 0.125 per cent iodocholeate.

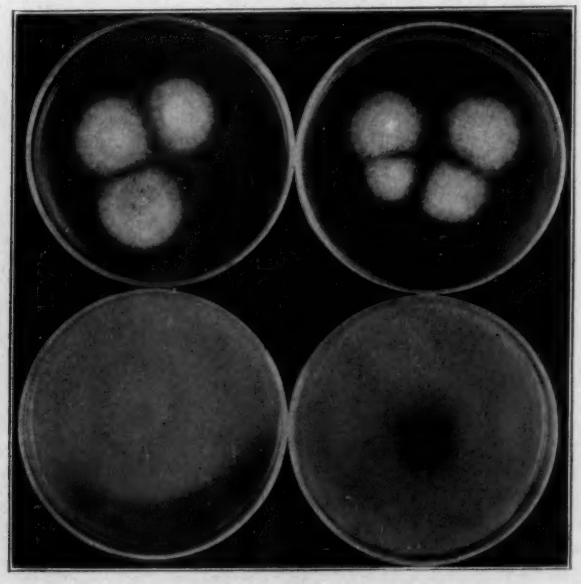


Fig. 4.—Cultures of Epidermophyton on Sabouraud's medium to which either tincture of iodine or iodocholeate was added. Upper row: left with 0.063 per cent and right with 0.042 per cent tincture of iodine; lower row: left with 0.063 per cent and right with 0.042 per cent iodocholeate.

0.083 per cent iodocholeate. In table 2 appear the results obtained in more than 350 cultures, showing that a lower concentration of iodocholeate than of tincture of iodine prevents the growth of fungi.

The Action of Iodocholeate Extends over a Longer Period than That of Tincture of Iodine.—This is because of the lower volatility of the iodine in iodocholeate and because it combines less readily with protein than the iodine in the tincture. It was shown that the fungicidal power of Sabouraud's medium containing iodocholeate remains about the same in the course of two weeks, while that of mediums containing tincture of iodine becomes less.

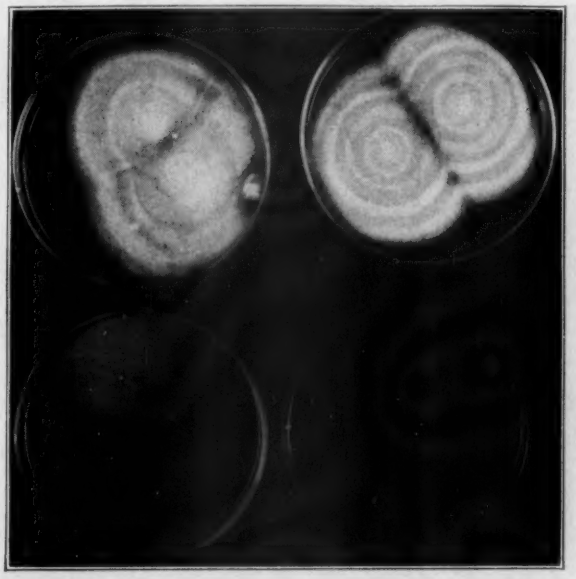


Fig. 5.—Cultures of Trichophyton on Sabouraud's medium to which either tincture of iodine or iodocholeate was added. Upper row: left with 0.125 per cent and right with 0.083 per cent tincture of iodine; lower row: left with 0.125 per cent and right with 0.083 per cent iodocholeate.

Sabouraud's medium was mixed with either 2.5 per cent iodocholeate or 2.5 per cent tincture of iodine in various amounts and then poured on Petri dishes. Half of the dishes were inoculated with fungi immediately and the others two weeks later. Table 3 shows that the minimal concentration of iodocholeate necessary to prevent growth of fungi remained the same, but the minimal concentration of tincture of iodine necessary to prevent growth changed for Microsporon from 0.167 to 0.25 per per cent; for Epidermophyton, from 0.083 to 0.125 per cent, and for Trichophyton, from 0.125 to 0.167 per cent.

Goedrich proved the lower volatility of iodocholeate as compared with tincture of iodine by the evaporation test. He showed that tincture of iodine loses most of its free iodine after standing a few minutes

TABLE 3.—*Results When Petri Dishes of Sabouraud's Medium with Addition of Either Iodocholeate or Tincture of Iodine in Various Concentrations Were Inoculated with Fungi*

	Growth with Given Concentration of Fungicide													
	Medium Inoculated Immediately							Medium Inoculated After 14 Days						
Fungus	0.25 %	0.167 %	0.125 %	0.083 %	0.063 %	0.042 %	0.031 %	0.25 %	0.167 %	0.125 %	0.083 %	0.063 %	0.042 %	0.031 %
With Iodocholeate Used as Fungicide														
Microsporon	—	—	+	..	..	..	..	—	—	+	..	..	..	..
	—	—	—	..	..	..	..	—	—	—	..	..	..	..
	—	—	—	..	..	..	..	—	—	—	..	..	..	..
Epidermophyton	..	..	—	—	—	+	+	..	..	—	—	—	—	+
	..	..	—	—	—	—	+	..	..	—	—	—	—	+
	..	..	—	—	—	—	+	..	..	—	—	—	—	+
Trichophyton	..	—	—	—	+	..	..	..	—	—	—	+	..	..
	..	—	—	—	+	..	..	..	—	—	—	+	..	..
	..	—	—	—	+	..	..	..	—	—	—	—	..	..
With Tincture of Iodine Used as Fungicide														
Microsporon	—	—	+	..	..	..	..	—	+	+	..	..	..	..
	—	—	+	..	..	..	..	—	+	+	..	..	..	..
	—	—	+	..	..	..	..	—	+	+	..	..	..	..
Epidermophyton	..	..	—	+	+	+	+	..	..	+	+	+	+	+
	..	..	—	—	+	+	+	..	..	—	+	+	+	+
	..	..	—	—	—	+	+	..	..	—	+	+	+	+
Trichophyton	..	—	—	+	+	..	..	..	+	+	+	+	..	..
	..	—	—	+	+	..	..	..	—	+	+	+	..	..
	..	—	—	+	+	..	..	..	—	—	+	+	..	..

Plus sign indicates growth; minus sign, no growth.

TABLE 4.—*Comparative Evaporation Test with Tincture of Iodine U. S. P. (7 per Cent) and Iodocholeate Solution (2.36 per Cent) at 37.5 C. (iodine content determined with hundredth-normal sodium thiosulfate; apparatus: Petri dishes)*

Material	Quantity, Cc.	Time, Min.	Iodine Retained (Total Percentage)
Tincture	0.1	5	1.49
Iodocholeate	0.1	5	70.10
Tincture	0.1	10	None
Iodocholeate	0.1	10	70.10
Tincture	0.2	10	1.06
Iodocholeate	0.2	10	98.20
Tincture	0.2	15	0.96
Iodocholeate	0.2	15	96.66
Tincture	0.2	30	0.003
Iodocholeate	0.2	30	92.53

in an open container at body temperature, while the content of free iodine in iodocholeate, as determined by titration with sodium thiosulfate, increases greatly, for the water evaporates, but not the iodine, which is adsorbed to the bile salt. With the permission of Dr. Goedrich, I include some of his results (table 4).

CLINICAL STUDIES

Because iodocholeate proved itself superior to tincture of iodine in laboratory studies, it was employed in the treatment of mycotic infections of the skin. The clinical results looked promising. It appeared that an improvement is obtained sooner than with other fungicidal agents such as sulfur-salicylic acid ointments, compound ointment of benzoic acid N. F. and mercurochrome. The fungicidal power of mercurochrome was found to be far below that of iodine or of iodocholeate. The average minimum concentration of mercurochrome in Sabouraud's medium necessary to prevent growth of Trichophyton was 1 per cent. (With 0.75 per cent growth occurred almost every time.) As shown previously, the necessary concentration of tincture of iodine is 0.125 per cent and of iodocholeate 0.083 per cent.

I used the clinical appearance of the lesions as the sole criterion of improvement, because it was found that the apparent disappearance of fungi from the lesions was an unreliable index. Often the fungi became undemonstrable after even indifferent treatment without clinical cure. In many cases of clinically clearcut mycotic infection I was unable to demonstrate the fungus, usually because the patient came under treatment after some time of self medication.

It was found that if iodocholeate ointment is used, the most desirable concentration is 2.5 per cent, whereas if the solution is used 1 per cent is often sufficient, as the solution brings the iodine in more intimate contact with the skin. When the disease is resistant the 2.5 per cent solution may hasten the improvement. Irritation was only occasionally observed after prolonged use of the 2.5 per cent solution. The solution has a more pronounced drying action than the ointment; therefore the choice of the ointment or the solution depended on the degree of drying and astringent effect desired. Especially good were the results in those mycotic infections in which there was maceration with oozing (often observed in epidermophytosis of the feet and hands), because of the drying and astringent effect of the iodocholeate solution. Both ointment and solution were applied three times a day. If the solution was used, no protecting bandage was necessary, as the solution dries soon on the skin, leaving a thin film. This is convenient when the patient is ambulatory. If the ointment was used, a bandage was applied. It proved valuable in some cases to use the solution twice during the day and the ointment at night. If the disease is in the acute inflammatory stage, however, or if there is secondary infection, it is well to treat the lesions for a few days with boric acid "soaks" or compresses before starting the iodocholeate treatment.

SUMMARY

Goedrich has discovered a new iodine compound, iodocholeate, which is an iodine-choleate adsorption compound. Because the iodine in iodocholeate is adsorbed to the bile salt, it is less volatile and combines less readily with protein. These two properties explain the advantages which iodocholeate has over tincture of iodine: 1. It is less irritating, as has been shown by patch tests. The ointment containing 2.5 per cent iodocholeate led to an erythematous reaction in 8 per cent of the cases and in no case to a vesicular reaction; the ointment containing 2.5 per cent tincture of iodine led to a reaction in 38 per cent (erythematous in 32 per cent and vesicular in 6 per cent). The 1 per cent iodocholeate solution led to an erythematous reaction in 6 per cent and in no case to a vesicular reaction; the 1 per cent tincture of iodine led to a reaction in 22 per cent (erythematous in 20 per cent and vesicular in 2 per cent). 2. Iodocholeate has greater fungicidal power than tincture of iodine in the presence of protein. A lower concentration of iodocholeate than of tincture of iodine is required in Sabouraud's medium to prevent the growth of fungi. As the human skin and its exudates contain protein, one might expect a higher fungicidal action here also. 3. Iodocholeate is active over a longer period than tincture of iodine. The fungicidal power of Sabouraud's medium containing tincture of iodine decreases in two weeks, while that of Sabouraud's medium containing iodocholeate remains the same. Either in solution or incorporated in an ointment iodocholeate has proved itself valuable in the treatment of fungous infections of the skin.

Dr. Paul Goedrich, of Rutgers University, New Jersey College of Pharmacy, Newark, N. J., furnished the iodocholeate used in these studies.

FIXED ERUPTION AND STOMATITIS DUE TO SULFANILAMIDE

ADOLPH B. LOVEMAN, M.D.
AND
FRANK A. SIMON, M.D.
LOUISVILLE, KY.

The literature is rapidly becoming voluminous with reports of various types of reactions following the use of sulfanilamide.[1] Although many of these have been cutaneous,[2] we have been unable to find any report of a fixed drug eruption. Rogers,[3] however, recently reported a most interesting case in which sulfanilamide taken by mouth provoked reactions at sites of previous injections of local anesthetics. The anesthetics injected had in common with sulfanilamide the base, aminobenzene. Noun [4] reported oral lesions following use of sulfanilamide, but his case is not absolutely beyond criticism, in that there was no attempt to reproduce the condition.

It is felt that since sulfanilamide is so universally employed, all proved unusual reactions should be recorded. This fact in addition to several unusual features in a case under observation has prompted the following report:

REPORT OF A CASE

History.—W. J., a man aged 34, was first seen in the department of dermatology and syphilology on Oct. 31, 1938, because of a cutaneous eruption accompanied

1. McGinty, A. P.: A Review of the Complications Following the Administration of Sulfanilamide, J. M. A. Georgia **27**:21 (Jan.) 1938. Ornsteen, A. M., and Fusit, W.: Peripheral Neuritis Due to Sulfanilamide, ibid. **111**:2103 (Dec. 3) 1938.

2. (*a*) Newman, B. A., and Sharlit, H.: Sulfanilamide: Photosensitizing Agent of Skin, J. A. M. A. **109**:1036 (Sept. 25) 1937. (*b*) Schonberg, I. L.: Purpuric and Scarlatiniform Eruption Following Sulfanilamide, ibid. **109**:1035 (Sept. 25) 1937. (*c*) Frank, L. J.: Dermatitis from Sulfanilamide, ibid. **109**:1011 (Sept. 25) 1937. (*d*) Myers, G. B.; Vonder Heide, E. C., and Balcerski, M.: Exfoliative Dermatitis Following Sulfanilamide, ibid. **109**:1983 (Dec. 11) 1937. (*e*) Finney, J. O.: Severe Dermatitis Medicamentosa Following Administration of Sulfanilamide, ibid. **109**:1982 (Dec. 11) 1937.

3. Rogers, E. B.: Sensitization Reaction to Sulfanilamide, J. A. M. A. **111**: 2290 (Dec. 17) 1937.

4. Noun, M. H.: Erosions of the Oral Mucosa and Urticaria of the Body Following Small Doses of Sulfanilamide, Arch. Dermat. & Syph. **37**:1044 (June) 1938.

with soreness of the mouth. On Sept. 14, 1938, he had been given sulfanilamide for gonorrheal urethritis. He took two 5 grain (0.32 Gm.) tablets three times a day for ten days, although the discharge disappeared at the end of five days. About four days after he stopped taking these tablets he noticed burning and itching on the left palm and the back of the neck and beginning soreness of the mouth. He described the cutaneous lesions as slightly elevated, purplish and about the size of a quarter. At the end of six or seven days the spots disappeared, leaving only brownish areas, which also left several days later. At the time he was taking no other type of medicine.

About a month later, on Oct. 28, 1938, there was a reappearance of the urethral discharge, and the following day he purchased some sulfanilamide tablets from the drugstore. He took three tablets three times that day and four times the following day (total of 7 Gm.). On the morning of the third day, October 31, the patient noted a recurrence of the "spots" in the same areas as before, accompanied by a severely sore mouth. In addition, three new areas became involved, one on the

Fig. 1.—Lesion on the back of the neck, beginning to exfoliate.

back of the right hand, one on the penis and one on the left leg, at a site at which a previous furuncle had been incised. As far as we could determine, no local anesthetic had been employed. He immediately discontinued sulfanilamide and entered the clinic for aid.

Examination.—The patient was rather poorly nourished and appeared about the stated age. He presented an eruption on the central portion and thenar eminence of the left palm, the penis, the back of the right hand, the back of the neck (fig. 1) and the lateral surface of the left leg, just below the level of the knee. Each lesion was about the size of a quarter except the ones on the midpalm and the penis, both of which were the size of a bean. All the areas were maculopapular and purplish red. The one on the thenar eminence had a large bleb superimposed (fig. 2). In addition, severe stomatitis was present on the lower lip (fig. 3), beneath the tongue and along the buccal mucous membrane. On the lip and beneath the tongue the lesions resembled closely the mucous patches of secondary syphilis. On each side of the buccal mucosa the mucous membrane was erythematous and raw looking, with a superimposed grayish white

membrane, some of which was hanging in shreds. This was the result of the rupture of bullous lesions. The involvement here was symmetric, and both above and below the involved areas normal mucous membrane could be seen.

Fig. 2.—Bullous lesion on the thenar eminence, as well as maculopapular lesion in the midpalm. The dark area near the former site is an artefact.

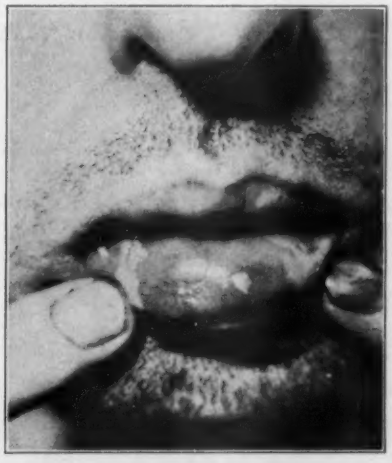


Fig. 3.—Character of the lesions on the lips. Note the resemblance to a mucous patch of secondary syphilis.

A clinical diagnosis of dermatitis medicamentosa and stomatitis medicamentosa was entertained.

Laboratory examinations at this time revealed nothing of significance. The Kahn and Kline tests were negative.

EXPERIMENTAL DATA

Reproducing the Eruption.—After all signs of the stomatitis and dermatitits had disappeared, the patient was given three 5 grain (0.32 Gm.) tablets of sulfanilamide by mouth, along with 1 Gm. of sodium bicarbonate. Three hours later he returned, complaining of burning of his mouth and itching of the palm and back of the neck. Examination at this time revealed no lesions in the mouth, but the areas on the left palm and back of the neck were definitely erythematous and sharply outlined. The next morning all previously involved areas had flared up, and there was a definite stomatitis, limited at first, however, to the left side of the buccal mucosa. By the following morning the patient had a severe stomatitis including the lower lip. This was similar in every detail to that originally seen, and was apparently also of a fixed nature, in that it recurred in the same areas after readministration of the drug.

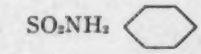
Additional Laboratory Data.—Complete blood studies made just prior to and eighteen hours after the administration of 1 Gm. of sulfanilamide showed insignificant changes, except an increase in the total white cell count, from 7,850 to 11,450.

Determinations of Blood Sulfanilamide.—The patient was given a single dose of 1 Gm. of sulfanilamide. Samples of blood were taken at two, four and twenty hours. At two hours the sulfanilamide concentration was 1.2 mg. per hundred cubic centimeters of blood; at four hours, 1.1 mg., and at twenty hours, 0.2 mg. These readings are normal.

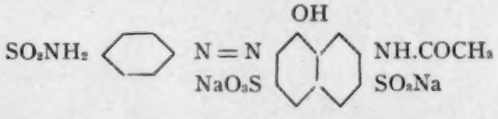
Administration of Neoprontosil.—It is claimed by the manufacturers that neoprontosil is less toxic than sulfanilamide and hence may often be tolerated when sulfanilamide cannot be taken.

The formulas for sulfanilamide and neoprontosil are furnished for comparison:

Sulfanilamide is paraaminobenzenesulfonamide.



Neoprontosil is disodium-4-sulfamidophenyl-2′-azo-7′-acetylamino-1′-hydroxynaphthalene-3′, 6′-disulfonate.



Accordingly, ten days after the administration of sulfanilamide, when all the signs of the eruption as well as the stomatitis had disappeared, the patient was given one 5 grain (0.32 Gm.) tablet of neoprontosil. About ten hours later he took three more tablets (1 Gm.).

On the following morning there was a flare-up in all the previously involved areas, but it was much less marked than the previous one. Although the mouth burned and felt somewhat uncomfortable, only slight erythema with a few erosive lesions could be seen.

The patient was seen again four days later, at which time there was still some evidence of residual erythema about the previously involved cutaneous areas. The mucous membranes, however, were entirely normal, and the patient volunteered the information that his mouth had not been nearly as sore after ingestion of these tablets as when he had taken the sulfanilamide. In addition to this intentional reproduction of the eruption and stomatitis, there were other recurrences when the patient took sulfanilamide of his own volition.

The fact that the patient could tolerate neoprontosil better than sulfanilamide may be of practical importance. It is probably due to the fact that the former preparation liberates less paraaminobenzenesulfonamide, and apparently it is to this portion of the complex chemical formula that the patient is sensitive.

Another interesting although expected feature in this case is that although a reaction could be elicited with both sulfanilamide and neoprontosil, the degree of local involvement was directly proportional to the dose administered. Small doses produced mild cutaneous reactions with only mild subjective oral symptoms, whereas large doses or repeated small doses produced a more severe cutaneous response (bullous type), along with a severe stomatitis. Unquestionably the stomatitis as well as the cutaneous reaction was of a fixed nature, because it also recurred in the same areas.

Patch Tests.—Usually patch tests in cases of fixed eruption give negative results, although positive reactions have been reported.[5] Positive reactions to patch tests with sulfanilamide have likewise occasionally been reported in other types of cutaneous disease.[2d] In the case under consideration tests were done with a 1 per cent aqueous solution of sulfanilamide on both normal and previously involved areas. Although these tests were performed several times, the patient returned only once for reading of the test and then at the end of forty-eight hours. At this time, however, there was a definite although mild reaction, evidenced by erythema on the previously involved area only. This was accompanied with local pruritus.

Local passive transfer was attempted by injection of 1.1 cc. of the patient's serum intradermally into each of 2 nonsensitive persons. Later

5. Loveman, A. B.: Experimental Aspect of Fixed Eruption Due to Alurate, a Compound of Allonal, J. A. M. A. **102**:100 (Jan. 13) 1934.

injection of sulfanilamide into these prepared areas of skin gave negative reactions, i. e., reactions no different from those produced by injection of sulfanilamide into unprepared sites in the same subjects.

SUMMARY AND CONCLUSIONS

Fixed eruptions and bullous stomatitis similar to those produced by phenolphthalein may be produced by sulfanilamide.

Patch tests gave positive results in previously involved areas but produced no reaction in areas of normal skin.

Although both the stomatitis and the fixed eruption could be reproduced with neoprontosil, the severity of the reaction was much less than with sulfanilamide.

Prof. Harry Carswell, of the Department of Chemistry of the University of Louisville Medical School, assisted in the construction of the chemical formulas, and Mr. J. D. McNeill, of Martin-McNeill Laboratories, made the determinations of sulfanilamide in the blood.

SARCOID OF BOECK

REPORT OF A CASE OF GENERALIZED CUTANEOUS DISTRIBUTION AND PULMONARY INVOLVEMENT, WITH CLINICAL CURE WITH TUBERCULIN

S. IRGANG, M.D.
NEW YORK

Much progress has been made in the study of sarcoid since Boeck [1] revealed this clinical entity. In addition to Boeck [2] dermatologists are indebted to Jüngling,[3] Schaumann,[4] Kuznitzky and Bittorf,[5] Kyrle,[6] Jadassohn [7] and many others for the attainment of a sound understanding of this disease.

It has been shown repeatedly [8] that the cutaneous eruption is merely a visible indication of a systemic disease, the tubercle bacillus being the

---

From the Department of Dermatology and Syphilology, Harlem Hospital.

1. Boeck, C.: Multiple Benign Sarcoid of the Skin, J. Cutan. & Genito-Urin. Dis. **17**:543, 1899.

2. Boeck, C.: (*a*) Fortgesetzte Untersuchungen über das multiple, benigne Sarcoid, Arch. f. Dermat. u. Syph. **71**:301, 1905; (*b*) Nochmals zur Klinik und zur Stellung des Miliarlupoid, ibid. **121**:707, 1916.

3. Jüngling, O.: (*a*) Ostitis tuberculosa multiplex cystica (eine eigenartige Form der Knochentuberculose), Fortschr. a. d. Geb. d. Röntgenstrahlen **21**:375, 1919; (*b*) Ostitis tuberculosa multiplex cystoides, zugleich ein Beitrag zur Lehre von den Tuberkuliden des Knochens, Beitr. z. klin. Chir. **143**:401, 1928.

4. Schaumann, J.: (*a*) Benign Lymphogranuloma and Its Cutaneous Manifestations, Brit. J. Dermat. **36**:515, 1924; (*b*) Observations cliniques, bactériologiques et sérologiques pour servir à l'étiologie de la lymphogranulomatose bénigne, Bull. Soc. franç. de dermat. et syph. (Réunion dermat., Strasbourg) **41**:1296, 1934; (*c*) Lymphogranulomatosis Benigna in the Light of Prolonged Clinical Observations and Autopsy Findings, Brit. J. Dermat. **48**:399, 1936.

5. Kuznitzky, E., and Bittorf, A.: Boecksches Sarkoid mit Beiteiligung innerer Organe, München. med. Wchnschr. **62**:1349, 1915.

6. Kyrle, J.: (*a*) Ueber die tuberkuloiden Gewebsstrukturen der Haut, Arch. f. Dermat. u. Syph. **125**:481, 1920; (*b*) Die Anfangsstadie des Boeckschen Lupoids: Beitrag zur Frage der tuberkulösen Aetiologie dieser Dermatose, ibid. **131**:33, 1921.

7. Jadassohn, J.: Remarks on Tuberculin in Dermatology, Brit. J. Dermat. **41**:451, 1929.

8. (*a*) Van Husen, J.: Ein Beitrag zur Kenntnis des Boeckschen Miliarlupoids und seiner Beziehung zu Erkrankungen anderer Organe, Dermat. Ztschr. **28**:1, 1919. (*b*) Rischin, M.: Universelles benignes Miliarlupoid Böck mit Beteiligung innerer Organe, Arch. f. Dermat. u. Syph. **139**:30, 1922. (*c*) Longcope, W. T., and Pierson, J. W.: Boeck's Sarcoid (Sarcoidosis), Bull. Johns Hopkins Hosp. **60**:223, 1937.

most likely inciting agent. Kyrle's [6b] success in demonstrating the presence of the tubercle bacillus in the early efflorescences in the banal inflammatory response and its gradual disappearance simultaneous with the onset of a tuberculoid histologic structure in mature lesions is undeniable evidence of tuberculous causation. These observations were confirmed by Ruete.[9] It thus became evident that the local immunologic response was capable of altering or destroying the micro-organism and hence preventing its detection in most instances. This frequent failure to detect the micro-organism prompted Longcope and Pierson [8c] to state recently that the cause of Boeck's sarcoid remains unknown, although they conceded that the consensus favors the tuberculous concept. Substantiating further this theory is Jüngling's [3b] inoculation of a guinea pig with positive results, the animal dying of tuberculosis. There is further suggestive evidence in Dittrich's [10] finding of acid-fast bacilli resembling the tubercle bacillus in 2 of his cases, Boeck's [2b] finding of acid-fast bacilli in nasal scrapings in 1 case and Sweitzer's [11] success in obtaining a microscopic reaction highly suggestive of tuberculosis in a guinea pig inoculated with sarcoid tissue.

The dermatologist is fully aware that infections such as leprosy, syphilis,[12] actinomycosis, trichophytosis [7] and leishmaniasis,[13] as well as the lymphoblastomas [14] and other malignant tumors [15] and subcutaneous injections of foreign substances [16] may induce a reaction microscopically simulating sarcoid. However, the clinical characteristics and the results of other pathologic examinations eventually eliminate the diagnosis from consideration.

Sarcoid is considered a tuberculous infection modified by an immunologic reaction of the tissue. The resultant altered state minimizes the infection for a variable period and transforms it into a comparatively

---

9. Ruete, A.: Zur Aetiologie der Boeckschen Erkrankung, Dermat. Ztschr. **37**:129, 1922.

10. Dittrich, O.: Ueber den direkten Tuberkelbazillennachweis beim Lupus pernio und beim Sarkoid Boeck, Dermat. Ztschr. **60**:395, 1931.

11. Sweitzer, S. E.: Sarcoid of Boeck, J. A. M. A. **63**:991 (Sept. 19) 1914.

12. Goeckerman, W. H.: Sarcoids and Related Lesions: Report of Seventeen Cases; Review of the Recent Literature, Arch. Dermat. & Syph. **18**:237 (Aug.) 1928.

13. Dupont, A.: Leishmaniose cutanée à structure histologique de sarcoïde de Boeck, Bull. Soc. franç. de dermat. et syph. (Réunion dermat., Strasbourg) **41**: 1291, 1934.

14. Zeisler, J.: An Uncommon Case of Multiple Benign Sarcoid of the Skin, J. A. M. A. **65**:764 (Aug. 28) 1915.

15. Nickerson, D. A.: Boeck's Sarcoid: Report of Six Cases in Which Autopsies Were Made, Arch. Path. **24**:19 (July) 1937.

16. Gougerot, H.: Sarcoïdes par corps étrangers, Bull. Soc. franç. de dermat. et syph. (Réunion dermat., Strasbourg) **41**:1370, 1934.

benign disease. In this disease none of the internal organs are exempt from attack. In the same patient, many viscera have shown characteristic pathologic alterations during the chronic course of this disease as a result of repeated hematogenous bacterial dissemination.[17] Pulmonary involvement is of particular interest not only because of its frequent association with cutaneous lesions but because it may simulate fatal miliary tuberculosis roentgenologically.

In the past, chronic miliary pulmonary tuberculosis reported cured was perhaps pulmonary sarcoid.[18] Stivelman and Hennell, in their discussion of this chronic disease, stated:

> A form of chronic pulmonary tuberculosis is not infrequently observed in which the miliary tubercules appearing in large numbers is an important element in the lesion. These may be confined to the upper lobes, but are most commonly found in the lower lobes. It is only rarely that one finds a chronic case in which the miliary tubercles are diffusely and uniformly scattered throughout both lungs. These cases of phthisis show clinical features and pursue a course which are at great variance with the ordinary acute type of this affection. They are more amenable to treatment, and they are subject to few exacerbations of activity. Furthermore, serial roentgenographic examinations of such cases may disclose not only a clearing of the collateral inflammation around the tubercles but also definite evidence of fibrosis and partial calcification of the tubercles themselves; and what is perhaps still more striking, there may occur apparent resolution in areas previously extensively involved.

The authors might have been dealing with pulmonary sarcoid and not with caseating tuberculosis as they had believed. The fact that these miliary lesions did not undergo destructive changes supports this contention.

Although a diagnosis of pulmonary sarcoid may be made from certain characteristics revealed by roentgen examination, the roentgenologist should not be expected to make the diagnosis from the roentgen data alone.[19] Inspection of the roentgenogram of pulmonary sarcoid [19a]

---

17. Bernstein, M.; Konzelmann, F. W., and Sidlick, D. M.: Boeck's Sarcoid: Report of a Case with Visceral Involvement, Arch. Int. Med. **44**:721 (Nov.) 1929. Spencer, J., and Warren, S.: Boeck's Sarcoid: Report of a Case with Clinical Diagnosis Confirmed at Autopsy, ibid. **62**:285 (Aug.) 1938. Pautrier, L. M.: La maladie de Besnier-Boeck, Presse méd. **43**:146, 1935. Reis, W., and Rothfeld, J.: Tuberculide des Sehnerven als Komplikation von Hautsarkoiden vom Typus Darier-Roussy, Arch. f. Ophth. **126**:357, 1931. Schaumann.[4a,c] Nickerson.[15]

18. Assmann, H.: Erfahrungen über die Röntgenuntersuchung der Lungen unter besonderer Berücksichtigung anatomischer Controllen, Jena, Gustav Fischer, 1914. Bodeker, F.: Ueber eine gutartige Form der disseminierten Lungentuberkulose (Tuberkulide der Lungen), Med. Klin. **28**:929, 1932. Stivelman, B. P., and Hennell, H.: Chronic Pulmonary Miliary Tuberculosis, J. A. M. A. **80**:536 (Feb. 24) 1923.

19. Kirklin, B. R., and Morton, S. A.: Roentgenologic Changes in Sarcoid and Related Lesions, Radiology **16**:328, 1931.

19a. Hantschman, L.: Ueber torpid Formen disseminierter Tuberkulose, Beitr. z. Klin. d. Tuberk. **73**:688, 1930.

will disclose linear striae extending from the hilus toward the periphery. These linear infiltrations extend in various directions, intersecting one another and forming a lacelike pattern. A variable number of small round shadows or nodules are observed both along these threadlike prolongations and at their intersections. The middle and lower half of each lung are affected. The apexes are rarely involved, and the signs of pleurisy and fluid are absent. The hilar and superior mediastinal lymph glands may or may not become involved. If they do enlarge, their shadows may resemble those of Hodgkin's disease or lymphosarcoma.

Anatomically, the nodules of sarcoid in the lung are essentially perivascular and are situated about the finer bronchioles and along the alveolar septums.[20] As in the skin, they are composed almost entirely of epithelioid cells with a sprinkling of small lymphocytes and Langhans giant cells. There is no inflammatory reaction in the surrounding tissue. Necrosis is absent.

The matter of mutation of the tubercle bacillus must receive serious consideration with reference to sarcoid. The investigations of Beinhauer and Mellon [21] have added renewed incentive to the study of the relation of nonvirulent non-acid-fast forms of this micro-organism to this disease. The lowering of tissue resistance may account for their reversion to the virulent, acid-fast state, thus explaining why sarcoid may in a small fraction of cases eventuate in progressive caseous tuberculosis and terminate fatally as pulmonary tuberculosis,[22] Addison's disease,[23] tuberculous meningitis [24] or renal tuberculosis.[25]

The purpose of this communication is to report a case of generalized cutaneous sarcoid with extensive pulmonary invasion which simulated fatal miliary tuberculosis roentgenologically. The excellent therapeutic result obtained with tuberculin perhaps adds another link in the chain of circumstantial evidence to support the tuberculous concept of this disease.

---

20. von Gebsattel, E.: Beitrag zum Verständnis atypischer Tuberkuloseformen, Beitr. z. Klin. d. Tuberk. **43**:1, 1919.

21. Beinhauer, L. G., and Mellon, R. R.: Pathogenesis of Noncaseating Epithelioid Tuberculosis of Hypoderm and Lymph Glands, Arch. Dermat. & Syph. **37**: 451 (March) 1938.

22. Funk, C. F.: Boecksches Sarkoid-Lupus Pernio und Lugenbeteiligung, Arch. f. Dermat. u. Syph. **167**:560, 1935. Grau, H.: Ergebnisse der Röntgenuntersuchung bei Lungentuberkulose, Beitr. z. Klin. d. Tuberk. **42**:327, 1919. Klingenstein, R.: Abgeheilte und Heilungs-Formen der generalisierten Tuberkulose mit Anteil der Lungen, Klin. Wchnschr. **5**:1310, 1926.

23. Seligsohn, F.: Beitrag zur Klinig der disseminierten Tuberkulosen, Beitr. z. Klin. d. Tuberk. **68**:485, 1928.

24. von Muralt, L.: Ueber Miliartuberkulose, Cor.-Bl. f. schweiz. Aerzte **46**: 481, 1916.

25. Assmann, H.: Internat. Zentralbl. f. d. ges. Tuberk-Forsch. **9**:54, 1915.

REPORT OF CASE

A Negress aged 23 was born and reared in South Carolina and had been a resident of New York city since 1928. There was no familial or personal history of either tuberculosis or syphilis. She was temperate as regards alcohol. She had never complained of any illness until five years before, when she contracted measles, which terminated uneventfully.

She had been in apparent good health until June 1936, when an ulcerating process developed on the vulva and two weeks later a slightly tender mass made its appearance on the lower right part of the flank, just above the iliac crest. The latter lesion ruptured spontaneously, discharging purulent material, and it required about nine months for complete resolution without surgical intervention and despite antisyphilitic therapy. This was probably a tuberculous abscess.

Fig. 1.—*A*, appearance of the cutaneous lesions prior to the institution of tuberculin therapy. A healed tuberculous abscess may be seen above the right hip. (Reproduced with the permission of Dr. Howard Fox.) *B*, photograph taken about four months later. Note complete resolution of the lesions, leaving pigmented atrophic scars. (Reproduced with the permission of the department of pathology, Harlem Hospital.)

On Nov. 23, 1936, she was admitted to one of the municipal hospitals, complaining of a discharging abscess and genital ulcerations which had been present for about five months. Donovan bodies were present in material from the genital lesions, and a routine Wassermann test of the blood gave a 4 plus result. The Frei test was negative. Examinations of urine and sputum likewise showed no abnormality.

She received antimony and potassium tartrate and antisyphilitic drugs. The granuloma inguinale responded well to treatment, but it was not entirely healed when she was discharged from the hospital on June 20, 1937, after a stay of seven months.

On June 30 she was admitted to the outpatient dermatologic department of the Harlem Hospital, where she continued to receive antisyphilitic drugs and antimony and potassium tartrate. During the first week of July 1937, a generalized eruption suddenly appeared. It was symmetric and nonpruritic and consisted of firm brownish papules and nodules, which were chiefly discrete, varied in size from that of a millet to that of a lima bean and were round, oval and even linear. Notwithstanding the fact that she had been receiving antisyphilitic treatment, the eruption was at first considered a secondary syphilid, but continuation of arsphenamine and bismuth therapy had no effect on the eruption. Later, when lesions began to appear on the inner canthi, alae nasi and vermilion border of the lips, the diagnosis of some type of tuberculosis became apparent. At no time

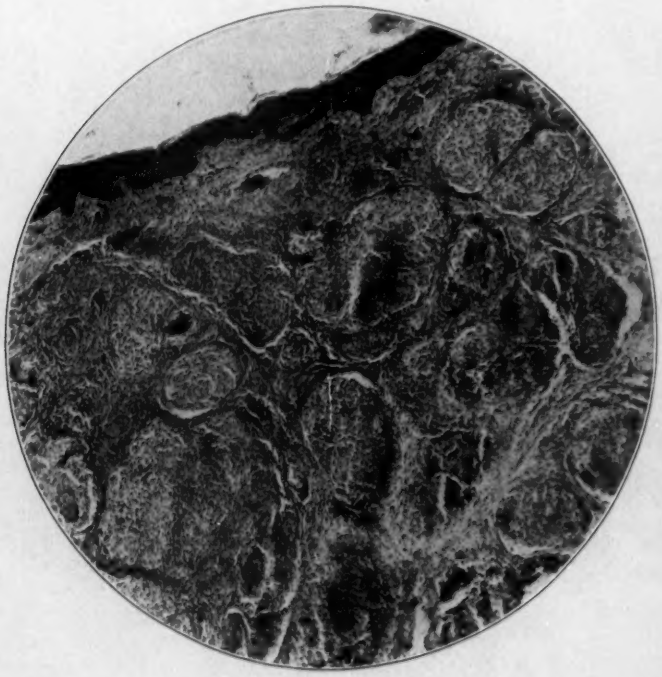


Fig. 2.—Low power photomicrograph, showing compact mass of epithelioid tubercles below the atrophic epidermis. The section was taken before the commencement of tuberculin therapy. (Reproduced with the permission of the department of pathology, Harlem Hospital.)

during the course of the disease did any of the lesions show the slightest evidence of breaking down. The liver and spleen were not palpable. Repeated Kahn tests of the blood were negative. Examination of the blood revealed only mild secondary anemia. A routine roentgen examination of the chest, spine, hands and feet showed no abnormality except in the chest. According to the roentgenologist, there was extensive miliary tuberculosis throughout both lungs, with enlargement of the mediastinal nodes. The patient felt perfectly well despite an afternoon rise of temperature to between 99.4 and 101 F. She did not complain of cough or weakness; there were no night sweats, and the appetite was good. After much persuasion the patient finally consented to a biopsy on Jan. 6, 1938.

On January 7, 0.1 cc. of old tuberculin in a dilution of 1 : 1,000,000 injected intracutaneously produced in forty-eight hours a pinkish red slightly edematous plaque about the size of a 10 cent piece. Injections of old tuberculin in 1.1 cc. doses were continued at first with a 1 : 1,000,000 dilution, but the dilution was later decreased to 1 : 100,000 and finally to 1 : 10,000, when the local cutaneous reactions to the tuberculoprotein became mild. Treatments were administered at intervals of from two to three weeks, depending on the time required for complete resolution of the preceding reaction. Focal reactions were not observed. At the patient's request, specific therapy was discontinued on September 16, 1938.

The cutaneous lesions showed evidence of resolution one week after the first injection of tuberculin. Healing continued at a slow pace until May 18, 1938,

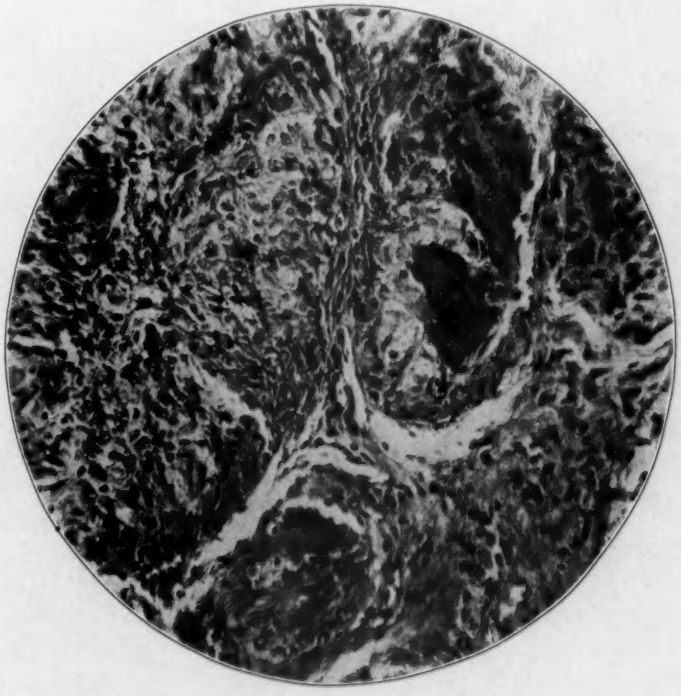


Fig. 3.—High power photomicrograph of the same section, showing Langhans giant cells in the epithelioid tubercles. Comparatively few lymphocytes may be seen scattered through the infiltrate. (Reproduced with the permission of the department of pathology, Harlem Hospital.)

when all cutaneous lesions had completely resolved, leaving superficial pigmented atrophic scars. A roentgenogram taken on May 19 showed disappearance of the pulmonary infiltration, but there was some evidence of enlargement of the mediastinal nodes. Another roentgenogram, taken on September 26, showed complete resolution of the original inflammatory process in both lungs and in the mediastinum. It required about four months to effect complete resolution of the cutaneous and pulmonary lesions.

Microscopic Examination of a Cutaneous Lesion.—A granuloma occupied almost the entire cutis, extending from the overlying atrophic epidermis to within a short

distance of the subcutis. It was sharply marginated and consisted of a compact mass of discrete and fused nodules, which were round, oval and cylindric. They were separated from one another by a framework of connective tissue. The tubercles consisted almost entirely of epithelioid cells, with a sprinkling of small lymphocytes and Langhans giant cells. The latter were noted chiefly in the infiltration on the fringes of this compact epithelioid mass. The nodules appeared to have a perivascular and perifollicular arrangement; this was particularly noted in the outlying infiltration. Moderate numbers of small lymphocytes and an occasional plasma cell were observed here. There was no evidence of necrosis in any of the tubercle formations. The microscopic picture was entirely consistent with the diagnosis of Boeck's sarcoid.

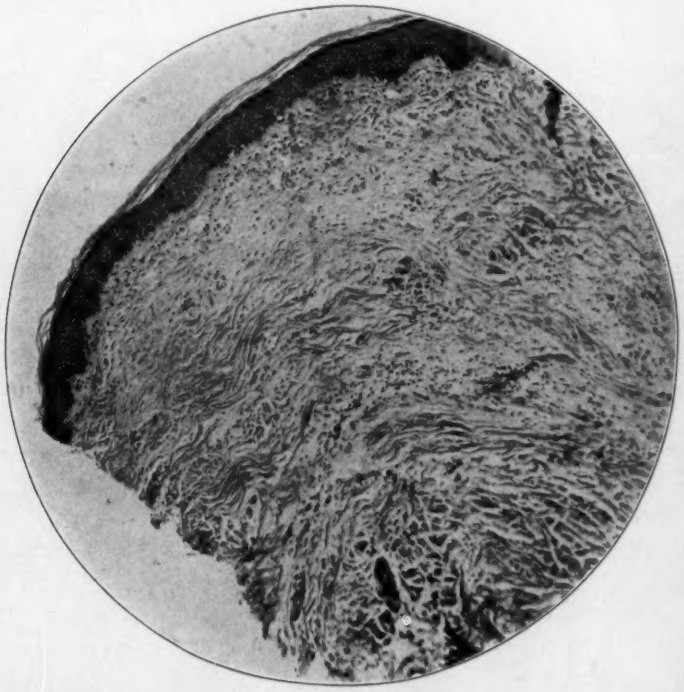


Fig. 4.—Low power photomicrograph of a section taken from an atrophic scar about four months after clinical healing. Note the distorted atrophic collagen fibers. The infiltrate has not been completely absorbed. The need for specific therapy long after the lesions have apparently healed becomes self evident. (Reproduced with the permission of the department of pathology, Harlem Hospital.)

As previously stated, sarcoid is considered a benign hematogenous form of tuberculosis. It is also considered to be more frequent in the Negro than in the white race, and when it does occur in the former, there is a decided tendency to more extensive distribution.

It is generally accepted that most patients with sarcoid are anergic to tuberculin. The incidence of positive reactions may vary with differ-

ent races, for it is not uncommon for the Negro to display a hyperergic state to tuberculoprotein. This fact may explain the divergence of opinion as regards the frequency of positive and negative reactions in this disease. Schaumann [4b] and Goeckerman [12] have expressed the belief that this reaction is practically always negative, while, on the other hand, Lomholt [26] obtained a positive reaction in 49 per cent of his cases and Kissmeyer [27] found the incidence of positivity as high as 40 per cent in the cases recorded in the literature. Jadassohn [7] stated that anergy is not constant even when the disease is typical.

Since sarcoid is usually refractory to the accepted empiric therapeutic agents, namely, arsenic, roentgen rays, radium, ultraviolet rays and solid carbon dioxide, it was decided to use tuberculin, because of the patient's allergic response to it and because Nomland [28] obtained an excellent result in a case of similar involvement. Since the results of specific therapy have been uniformly unfavorable when the patient is anergic, it should be attempted only for those who react positively to a dilution of 1:1,000 or greater. In my limited experience, the most satisfactory results have been obtained when the local reaction is characterized forty-eight hours after injection by a pinkish red slightly edematous plaque measuring from ¼ to ½ inch (0.6 to 1.3 cm.) in diameter. Focal reactions should be avoided. The injection is repeated when the preceding reaction subsides completely; this occurs within two or three weeks. Treatments should be continued for some time after entire resolution has been effected.

Both treated and untreated, Boeck's sarcoid has an extremely variable course. It may persist for years regardless of therapy, yet at rare intervals spontaneous resolution has taken place without therapeutic intervention. In the case presented, the eruption persisted for about six months without the slightest evidence of resolution, despite energetic arsphenamine and bismuth medication, yet one week after the first intracutaneous injection of tuberculin signs of healing were noted. This fact indicates strongly that tuberculin was directly responsible for the clinical cure in this case.

SUMMARY AND CONCLUSIONS

Sarcoid of Boeck is a systemic infection, the tubercle bacillus being the most likely etiologic agent.

No organ is immune from attack. Pulmonary involvement is of particular interest because it simulates fatal miliary tuberculosis roentgenologically.

---

26. Lomholt, S.: Sur des lésions muqueuses dans les sarcoïdes, Bull. Soc. franç. de dermat. et syph. (Réunion dermat., Strasbourg) **41**:1142, 1934.

27. Kissmeyer, A.: Clinical Aspect and Etiology of Boeck's Sarcoid, Hospitalstid. **74**:1047, 1931.

28. Nomland, R.: Hematogenous Cutaneous Tuberculosis (Sarcoid) in Negroes: Report of Six Cases, Arch. Dermat. & Syph. **30**:59 (July) 1934.

Sarcoid is considered more frequent in the Negro. It is usually more extensive in this race, at least from the standpoint of cutaneous involvement.

The mutation of the tubercle bacillus must receive serious consideration. The dissociants of this micro-organism may be responsible for the clinical entity of sarcoid. The theory of mutation may explain the rare instances of fatal termination.

Patients with sarcoid react positively at times to intracutaneous injections of tuberculin. The Negro has a tendency to hyperergy to this substance.

Since the patients are often refractory to empiric therapeutic measures, tuberculin therapy should be tried for those who display an allergic response to a dilution of 1 : 1,000 or greater.

A case is described in which a clinical cure was accomplished with specific therapy.

THE LAUGHLEN TEST

IN THE DIAGNOSIS OF SYPHILIS

WALTER F. LEVER, M.D.
AND
WILLIAM K. MASSIE, M.D.
BOSTON

The desirability of a serologic test for syphilis more rapid and more easily performed than any at present available at the Massachusetts General Hospital, to be used in the outpatient clinic and for the testing of emergency donors, gave the incentive for a comparative study of the Laughlen test with the tests now in use, i. e., the Hinton, the Wassermann and the Kahn.

The Hinton test is used as a routine at the Massachusetts General Hospital on all specimens of serum sent to the laboratory. The less sensitive standard Wassermann test rather than the Kolmer modification is performed on the serums giving a positive Hinton reaction, in order to grade the more strongly positive ones. The Kahn test is done in emergencies. The technics of these tests are too well known to require description. In the present study the rapid Hinton method was used in 780 cases. This test is performed like the standard Hinton, except that the time of incubation is reduced from overnight to half an hour and the incubated material is centrifuged for ten minutes. Any positive granules will collect at the meniscus during this procedure.

Though the Laughlen test has been described in detail by its originator,[1] it is less well known than the other tests. It seems fitting that the procedure be described briefly, with the addition of such details as were found helpful in this study.

TECHNIC OF THE LAUGHLEN TEST

The Laughlen reagent, which is a precipitation antigen to which cholesterol, balsam and scarlet red have been added must be activated at least twenty-four hours prior to use by the addition of 10 per cent sodium chloride in amounts specified with each sample.

1. Whole blood is centrifuged and the serum obtained.

2. The serum is inactivated in a water bath at 55 C. for thirty minutes. (Inactivation at approximately 63 C. for three minutes, though not used routinely, was found compatible with accuracy in isolated examinations.)

From the Department of Dermatology and Syphilology and the Department of Pathology and Bacteriology, Massachusetts General Hospital.

1. Laughlen, G. F.: A Rapid Test for Syphilis, Canad. M. A. J. **33**:179, 1935.

3. A slide is heated gently and divided with a blue wax pencil into five sections. Three loopfuls of serum are placed with a 5 mm. platinum loop in each section. (If a larger area of the slide is used, the rate of drying is increased, and as drying leads to formation of granules, a normal specimen may give a reaction appearing weakly positive.)

4. One drop of activated antigen is added from a capillary pipet to each section. (The combined amount of fluid should be large enough not to show evidence of drying during the ten minutes of shaking and not so large as to drop from the slide when it is oscillated. The amount of antigen should be larger than the amount of serum, as it was found that slight granulation occurs in some normal specimens if too little antigen is added.)

5. The slide is oscillated from side to side at least forty times every three minutes and the test read after ten minutes. If the drop has retained the homogeneous translucent pink color, the test is negative. If there are red granules in a clear fluid, the test is positive. (The test is read by holding the slide perpendicularly in a strong light and looking through it toward a dark background. Except with specimens giving weakly positive reactions, large granules will appear within the first five minutes. These may show only slight granulation in ten minutes. Careful comparison with a known normal control is essential. In a few of the normal specimens fine granules are present in the film above the drop, but the drop presents the homogeneous translucent appearance. Only when the drop shows definite granulation with simultaneous clearing should the test be called positive.)

A fact well appreciated by any one familiar with precipitation tests is the ease with which the strongly positive reactions can be detected and the difficulty encountered in reading weakly positive reactions. Accurate judgment of any test can be acquired by experience only. The dividing line between positive and negative is perhaps less definite and can be influenced by more factors with the Laughlen test than with the Hinton or the Kahn. The variable factors of significance are: (1) the relative amount of inactivated antigen to sodium chloride, (2) the relative amount of activated antigen to serum, (3) the amount of drying and (4) the amount of shaking. We feel that one must have performed a large number of tests (at least 500) on known samples to acquire any degree of accuracy.

SUMMARY OF THE LITERATURE

Laughlen in his original paper [1] published two series of results, one obtained by himself and one at another hospital in Toronto, Canada. In his series of 400 specimens, the Laughlen reaction was in agreement with the Wassermann in 98 per cent and with the Kahn in 99 per cent. In the other series (118 syphilitic specimens) the Laughlen reaction agreed with the Wassermann in 93.5 per cent of cases and with the Kahn in 97 per cent. Price [2] found the Laughlen test more sensitive than the Kolmer-Wassermann and as sensitive as the Kahn. He obtained no false positive results with a series of 90 normal specimens.

2. Price, A. S.: The Laughlen Agglutination Test for the Serological Diagnosis of Syphilis, M. Times, New York **65**:398, 1937.

In Robinson and Stroud's [3] series of 1,000 tests, the Laughlen test agreed with the Wassermann in 93 per cent and with the Kahn in 97 per cent, a result identical with that of Laughlen's second series. These authors reported no false positive reactions. Usher,[4] in an attempt to verify Laughlen's statement that the test "can be done by any medical practitioner or technician without special training," performed, without previous experience, the Laughlen test on a series of 181 normal specimens of blood and found 3.8 per cent false positive and 6.7 per cent doubtful reactions. By decreasing the sodium chloride content of the activated antigen he so standardized his antigen as to reduce the number of false positive results, but simultaneously reduced the sensitivity. At a point where no false or doubtful positive reactions were obtained, the sensitivity was still equal to that of the Eagle test performed on the same specimen. This is of no practical importance, however, as each operator cannot standardize his antigen before using it, and we are in accord with Usher's conclusion and with Moore's editorial comment [5] that the use of this test by inexperienced workers "is to be strongly condemned." [6] Rein and Hazay [7] found 2.33 per cent false positive Laughlen reactions in a series of only 215 normal specimens, and a sensitivity of 95 per cent in a series of 400 known syphilitic specimens. The Kline test gave no false positive results and showed a sensitivity of 99 per cent. They expressed the belief that the Laughlen test is an adequate exclusion test in emergency work, but because of the occurrence of 2.33 per cent false positive results they did not recommend it for other diagnostic purposes. Dienst and Sanderson [8] tested 276 specimens of serum obtained from patients with a history of active syphilis and found the Laughlen reaction positive in 96.3 per cent, the Kahn in 93.4 per cent and the Wassermann in 77.8 per cent.

SEROLOGIC STUDIES AT THE MASSACHUSETTS GENERAL HOSPITAL

The 3,000 tests performed were divided into two series.

First Series.—In the first series, 2,220 tests were performed on routine samples: Hinton and Laughlen tests were made on all speci-

3. Robinson, F. H., and Stroud, G. M.: Laughlen's Test for the Serodiagnosis of Syphilis, J. A. M. A. **108**:1170 (April 3) 1937.

4. Usher, G. S.: An Appraisal of the Laughlen Serologic Test for Syphilis, Am. J. Syph., Gonor. & Ven. Dis. **22**:452, 1938.

5. The Laughlen Test for Syphilis, editorial, Am. J. Syph., Gonor. & Ven. Dis. **22**:517, 1938.

6. We performed more than 800 tests, checking the results carefully with the routine Hinton test, prior to tabulating any figures included in our report.

7. Rein, C. R., and Hazay, C. E.: The Laughlen Test for Syphilis, J. Invest. Dermat. **1**:283, 1938.

8. Dienst, R. B., and Sanderson, E. S.: The Laughlen Test as Compared to the Kahn and Modified Kolmer Serodiagnostic Tests for Syphilis, Am. J. Syph., Gonor. & Ven. Dis. **22**:699, 1938.

mens, but the Wassermann test was performed only on those in which the Hinton or the Laughlen reaction was positive. Among these 2,220 specimens 442 were presumptively syphilitic and 1,778 nonsyphilitic. As presumptively syphilitic were classified all specimens from patients with

TABLE 1.—*Classification of the Four Hundred and Forty-Two Syphilitic Specimens of the First Series*

Laughlen Successful				Laughlen Failed		Total
1	2	3	4	5	6	
Hi +	Hi +	Hi −	Hi −	Hi +	Hi +	
Wa +	Wa −	Wa +	Wa −	Wa +	Wa −	
L +	L +	L +	L +	L −	L −	
			History of syphilis	Missed Wa	Missed Hi	
168	157	8	3	14	92	442

* Hi designates Hinton reaction; Wa, Wassermann; L, Laughlen.

TABLE 2.—*Results of Tests in Both Series, Separately and Compiled*

	Group A Presumptively Syphilitic (Positive Hinton and those with a negative Hinton if there was a history of syphilis)					Group B Known Syphilitic (More than one blood test positive or a history of syphilis)				
First series: 442 specimens, 50 of which had a positive Hinton test only and were from patients with no history of syphilis						First series: 392 specimens				
	Hi	RH	L	Ka	Wa	Hi	RH	L	Ka	Wa
No. of positive reactions..	431	...	334	...	189	381	...	334	...	189
Percentage positive.....	97.5	...	75.6	...	42.8	97.2	...	85.2	...	48.2
Second series: 390 specimens, 31 of which had a positive Hinton test only and were from patients with no history of syphilis						Second series: 350 specimens				
	Hi	RH	L	Ka	Wa	Hi	RH	L	Ka	Wa
No. of positive reactions..	383	371	300	268	177	352	345	300	268	177
Percentage positive.....	98.2	95.1	76.9	68.7	45.4	98.1	96.1	83.6	74.7	49.3
Both series: 832 specimens, 81 of which had a positive Hinton test only and were from patients with no history of syphilis						Both series: 751 specimens				
	Hi	RH	L	Ka	Wa	Hi	RH	L	Ka	Wa
No. of positive reactions..	814	...	634	...	366	733	...	634	...	366
Percentage positive.....	97.8	...	76.2	...	44.0	97.6	...	84.4	...	48.7

* RH designates rapid Hinton test; Ka, Kahn test.

a positive Hinton test (431) and from those with a negative Hinton test who offered a history of syphilis (11) (table 1). Of the 442 presumptively syphilitic specimens of serum, the Hinton reaction was positive in 431 (97.5 per cent), the Laughlen in 334 (75.6 per cent) and the Wassermann in 189 (42.8 per cent) (table 2, group A, series 1).

In 92 of the 442 specimens in the first series only the Hinton reaction was positive. These 92 specimens are classified in table 3.

Forty-two specimens (46 per cent) were from patients with evidence of syphilis (either syphilitic lesions or a history of syphilis). Twenty-three specimens (25 per cent) were from persons with no history of syphilis, and 27 could not be classified, as they were for the most part obtained from transfusion donors without a hospital history; these 50 specimens, then, must be considered unknown. In group B of table 2, the percentage rating of the three tests is calculated on the basis of 392 specimens, which merely excluded the 50 "unknown" specimens. The actual rating must lie somewhere between the two values set down in this table. It is impossible to be more specific.

The number of false positive Laughlen reactions in this series was 0.7 per cent—in 13 of 1,778 normal specimens (table 4). A number of these were borderline reactions and when the test was repeated were read as negative (table 4).

TABLE 3.—*Classification of One Hundred and Thirty-Four Presumptively Syphilitic Specimens in Which the Hinton Reaction Only Was Positive*

	History of Syphilis	History of Syphilis But Two or More Negative Hinton Tests in the Past	Unclassifiable	No History of Syphilis
First series	29	13	27	23
Second series	9	2	8	23
Total	38	15	35	46
Percentage	28.4	11.2	26.1	34.3

Although the Hinton test is one of the best tests in use,[9] it has one disadvantage, brought out in this investigation, which can lead to

9. According to the paper by H. S. Cumming, H. H. Hazen, A. H. Sanford, F. E. Senear, W. M. Simpson and R. A. Vonderlehr (The Evaluation of Serodiagnostic Tests for Syphilis in the United States: Report of Results, J. A. M. A. **104**:2083 [June 8] 1935), reporting on the investigation of the most widely used tests through the United States Public Health Service, the Hinton test showed a sensitivity of 86 per cent and a specificity of 99.3 per cent (0.7 per cent false positive reactions). Other tests obtained the following ratings: Eagle, 84.1 per cent sensitivity and 98 per cent specificity; Kahn, 80.5 per cent sensitivity and 100 per cent specificity; Kline, 76.3 per cent sensitivity and 100 per cent specificity; Kolmer, 75.4 per cent sensitivity and 100 per cent specificity. According to the paper of N. Nagle and S. C. Willet (What Did Five Official Evaluation Studies for Syphilis Reveal? Am. J. Syph., Gonor. & Ven. Dis. **22**:231, 1938), the Hinton test is the most sensitive of all six tests investigated (Kahn, Eagle, Kolmer, Kline, Hinton and Johns), rating 87 per cent in the laboratory of Hinton himself and 90 per cent in independent laboratories. In Hinton's laboratory 1.4 per cent false positive results occurred, and there were none in the other laboratories. In the series of the United States Public Health Service of September 1938, the Hinton test again proved to be the most sensitive test evaluated (sensitivity 83.9 per cent) and had a specificity of 100 per cent. These figures were obtained by special communication and were not in print when this paper was submitted for publication.

serious consequences. Among the 11 syphilitic specimens with a negative Hinton reaction, 3, 0.7 per cent of all syphilitic specimens, were from patients with clinical signs of syphilis and strongly positive Wassermann and Laughlen reactions: 1 with early secondary syphilis and positive results on dark field examination, 1 with multiple ulcerated gummas on the leg and 1 baby 3 months of age with periostitis syphilitica, chorioretinitis syphilitica and a strongly positive Wassermann reaction of the spinal fluid. In the case of the baby, eight Hinton tests in a few weeks' interval were all negative; in the other 2 cases, three Hinton tests were negative and none positive. However, in all 3 cases the Hinton test was positive when done with dilutions. Hence, it is advisable in all cases of a negative Hinton test and a strong suspicion of syphilis to make the test with dilutions or to check the result with another test.

Second Series.—After this series of 2,220 tests was completed, it seemed advisable to extend the investigation to other rapid tests and to obtain a check on the figures in the first series. Therefore, a second

TABLE 4.—*False Positive Reactions Obtained on Normal Specimens*

	First Series 1,778 Normal Specimens		Second Series 390 Normal Specimens		Total 2,168 Normal Specimens	
	No.	%	No.	%	No.	%
Laughlen	13	0.7	3	0.8	16	0.7
Kahn	..	...	0	0.0		
Rapid Hinton	..	...	8	2.1		

series, of 390 presumptively syphilitic specimens of serum and 390 normal specimens, was tested by the Hinton, the Wassermann, the Laughlen, the Kahn and the rapid Hinton method. In this series again specimens were designated as presumptively syphilitic when they came from patients with a positive Hinton reaction (383) or from those with a negative Hinton reaction who reacted positively to two or more other tests or offered a history of syphilis (7). As shown in table 2, group A, series 2, in which calculations were made on the 390 presumptively syphilitic specimens, the Hinton reaction was positive in 383 (98.2 per cent), the rapid Hinton in 371 specimens (95.1 per cent), the Laughlen in 300 (76.9 per cent), the Kahn in 268 (68.7 per cent) and the Wassermann in 177 (45.4 per cent). Forty-two of the 390 presumptively syphilitic specimens showed a positive Hinton reaction only (either standard Hinton or standard and rapid Hinton). Eleven of those (27 per cent) were from patients with a history of syphilis and 23 (55 per cent) from persons with no evidence of syphilis; 8 (18 per cent) could not be classified for lack of history (table 3, second series). Counting the known syphilitic specimens only (359), the 23 from patients with a positive Hinton reaction only and no history of syphilis and the 8 unclassified

ones being excluded, we found these comparative data (table 2, group B): The Hinton reaction was positive in 352 (98.1 per cent), the rapid Hinton in 345 (96.1 per cent), the Laughlen in 300 (83.6 per cent), the Kahn in 268 (74.7 per cent) and the Wassermann in 177 (49.3 per cent). Just as in the first series, it is not possible to say which set of figures (group A or group B) more closely approached the true values, which lay somewhere between the figures presented in the two groups.

Among the 390 normal specimens there were 3 with a positive Laughlen reaction (0.8 per cent) and 8 with a positive rapid Hinton reaction (2.1 per cent). The Kahn test revealed no false positive results (table 4).

Comparison.—A comparison of the two series shows rather close correlation. If the figures of both series are summed up, the following results for Hinton, Laughlen and Wassermann tests (as only those tests were done in both series) are obtained (table 2):

Group A (comprising all presumptively syphilitic specimens): Total, 832; Hinton positive, 814 (97.8 per cent); Laughlen positive, 634 (76.2 per cent); Wassermann positive, 366 (44 per cent).

Group B (comprising known syphilitic specimens only, i. e., either two or more different blood tests were positive or the patient had a syphilitic history): Total, 751; Hinton positive, 733 (97.6 per cent); Laughlen positive, 634 (84.4 per cent); Wassermann positive, 366 (48.7 per cent).

The Laughlen test gave 16 false positive results among 2,168 normal specimens, giving an average specificity of 99.3 per cent.

As the survey of tests for syphilis carried out by the United States Public Health Service is generally regarded as the official rating, an attempt has been made to correlate the Laughlen test with this rating. For comparison, the last survey, carried out in September 1938, is used. This gave the Hinton test a rating of 83.9 per cent for sensitivity. As the tests of the United States Public Health Service were done on known syphilitic specimens, only the tests with the "known syphilitic" specimens of the two series of this paper are used for the comparison (that is, group B). Of the 751 specimens comprising group B, the Hinton reaction was positive in 97.6 per cent, the Laughlen in 84.4 per cent and the Wassermann in 48.7 per cent (table 2, group B). Correcting, then, on the basis of a rating of 83.9 per cent for the Hinton test places the rating of the Laughlen test at 72.5 per cent and that of the Wassermann test at 41.9 per cent. The rating of the Kahn test (based on the second series only) would be 63.9 per cent.

COMMENT

The Laughlen test is fast and easy to perform. Fifteen to twenty minutes after the blood has been taken the result can be known. Little laboratory equipment is needed. Its sensitivity (76.2 per cent) and

specificity (99.3 per cent) make it a test which can be used safely for emergency work (as on blood donors) and in syphilitic outpatient departments, where a blood test done in a few minutes' time to support the clinical diagnosis is desirable. The Hinton test is more sensitive than the Laughlen, but requires twelve hours for completion. The rapid Hinton test, only slightly less sensitive than the standard Hinton, is more sensitive than the Laughlen test. However, it requires forty-five to sixty minutes to perform and is not suitable for use in outpatient departments because of the laboratory equipment required. Its low specificity (97.9 per cent) in our hands limits its usefulness. The Kahn test has a comparatively low sensitivity, but a specificity of 100 per cent. It is comparable to the rapid Hinton test in difficulty of performance and equipment required.

It is felt that the Laughlen test deserves more attention than it has so far been given by serologists and syphilologists. The opposition to the Laughlen test has developed out of the incautious statement of Laughlen that the test "can be done by any medical practitioner or technician without special training." This, in our experience, is incorrect. There is no test, to our knowledge, which does not require extensive experience, and as far as the Laughlen test is concerned, it has been stated before that borderline reactions are even slightly more difficult to interpret than with the corresponding Hinton and Kahn tests.

SUMMARY

1. The technic of and the literature on the Laughlen test have been reviewed.

2. A series of 2,220 Laughlen tests have been compared with the Hinton and the Wassermann test.

3. A series of 780 Laughlen tests have been compared with the Hinton, the rapid Hinton, the Wassermann and the Kahn test.

4. The Laughlen test has been found to be easy and fast (fifteen to twenty minutes to perform). The reading of the test is relatively easy for those who have had experience with it.

5. The sensitivity and specificity of the Laughlen test warrant its use as an emergency test in preference to any other test performed on this series.

6. Compared with two other rapid tests, the Laughlen test was found less sensitive but more specific than the rapid Hinton and less specific but more sensitive than the Kahn test.

UNRECTIFIED X-RAY MACHINES FOR DERMATOLOGIC USE

CLINICAL CONSIDERATIONS

JULIUS E. GINSBERG, M.D.
CHICAGO
AND
ROBERT S. LANDAUER, PH.D.
HIGHLAND PARK, ILL.

During the past several years there has been an increasing use of small unrectified x-ray machines by dermatologists. This type of equipment has been used over a period sufficiently long to permit evaluation, and we feel that a critique would be of value to dermatologists contemplating purchasing new machines in the near future.

The several types of x-ray apparatus available for treatment may be classified in the following groups: full wave rectified, either mechanically or by means of four valve tubes; half wave suppressed by means of one or two valves, and half wave suppressed (so-called unrectified) by means of the x-ray tube itself. An understanding of what rectification is and why it is employed is necessary to an intelligent understanding of the problem. There is still a rather widespread impression among both radiologists and dermatologists that a machine with an unrectified circuit is unsuitable for treatment. This impression is erroneous. The radiation produced by an x-ray tube, is, for all practical purposes, unrelated to the type of electrical circuit employed in energizing it, whether rectified or not. The need for rectification or wave suppression lies wholly in the inability of certain types of x-ray tubes to operate satisfactorily without it. The process of rectification consists in the conversion of the pulsating alternating current delivered by the high tension transformer into pulsating direct current. This conversion may be accomplished either with a mechanical switch operating synchronously with the alternations of the transformer [1] or with valve tubes arranged in a proper electrical circuit. When a mechanical rectifier or four valve tubes are used, both halves of the alternations of the current are utilized by

1. Dr. G. M. MacKee, in his recent book X-Rays and Radium in the Treatment of Diseases of the Skin (Philadelphia, Lea & Febiger, 1938), pointed out that the electrical or thermionic method of rectification has many advantages over the mechanical and that, in spite of improvements, mechanical rectifiers are rapidly becoming obsolete.

the x-ray tube (fig. 1 *B*). When one or two valves or none at all are used, the current is not rectified but simply has one half of its alternations suppressed (fig. 1 *C*).

The principle of operation of an x-ray tube is the emission from a hot negative element (called the filament) of negative electrons, which are then accelerated by a high voltage so that they strike a metal plate (called the target), with the subsequent formation of roentgen rays. Nothing inherent in this process necessitates rectification. From a practical standpoint, however, if the target becomes heated to incandescence by the impact of the electrons, it will when negative emit electrons itself. These electrons will then be accelerated to the filament, and x-rays will be generated at the filament. Since the filament is not designed for this service, it would quickly be destroyed by this action. Hence

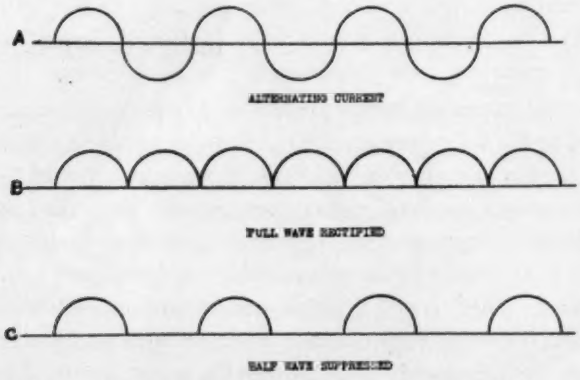


Fig. 1.—Representation of alternating current: *A*, unaltered; *B*, with full wave rectification, and *C*, with half wave suppression.

it is necessary to rectify the current or to suppress the negative half wave so that the target never becomes negative, for so long as it is positive it cannot emit electrons. This is the so-called Edison effect: a hot body in order to emit electrons must be charged negatively. Thus if the target of the x-ray tube is of such design that it will get incandescent when the tube is working, some means (called rectification) must be taken to prevent its ever becoming negatively charged. This is the sole reason for rectification. There is no difference in the x-rays produced whether the current is or is not rectified. If, however, the target is or can be designed so that it will not become incandescent when the tube is being operated, it is not necessary to rectify the current, for according to the Edison effect, a cool body even though negatively charged will not emit electrons, and hence no reverse flow of electrons to the filament can occur. Targets can be designed which by the use of radiating fins or by water cooling will remain cool during operation

X-ray tubes containing such targets may be operated satisfactorily without rectification and are called radiator tubes. To recapitulate: The need or lack of need for rectification is based solely on the design of the x-ray tube. The kind of x-rays produced and their biologic action are not dependent on rectification.

In that group of x-ray machines which employ one or two valves only half of the alternating current wave is utilized; the other half is suppressed. The electrical characteristics of the circuit are similar to those of the circuit employing no valves but only the x-ray tube. However, since the valve or valves, rather than the x-ray tube, suppress the wave the target of the latter may be allowed to become incandescent. The valves keep it from becoming negatively charged, and hence, even if it does get hot, it can never emit electrons. Thus, with this type of circuit either the old style "hot" target or the radiator type may be used. There is little to be gained by the use of one or two valves, except this greater freedom in the choice of the x-ray tube and a problematic greater life for the tube.

The advantages to the dermatologist in the use of an unrectified machine are numerous:

1. Low initial cost.
2. Low upkeep (no motor or valves to repair).
3. No noise. (Some unrectified machines actually have buzzers installed so that the operator may know when the current is on.)
4. Small space requirements.
5. Simple installation and ease of moving to new quarters.
6. No radio interference.

At the same time, there are certain disadvantages, the two principal ones being:

1. Greater electrical danger unless shockproof tubes are used.
2. Time limitation of operation.

The advantages are so obvious that no explanation need be made regarding them. The disadvantages need explaining. Since unrectified machines are constructed without resistance control, they are more dangerous in case of accidental short circuit than are rectified machines, which are usually at least partially rheostat controlled. We strongly recommend that dermatologists do not use unrectified machines for routine treatment unless they are fitted with shockproof tubes and cables.

The rectified machine and its hot anode tube may be operated continuously at 5 milliamperes and at voltages higher than the dermatologist ever uses—for twenty-four hours a day if necessary. With the unrectified machines with radiator tubes—or, as a matter of fact, with a

radiator tube on any type of circuit—there is a definite time limitation varying from three to twenty minutes, depending on the particular tube used and due to the fact that the target gets too hot. This statement must be amended to exclude two tubes which owing to water cooling may be operated continuously. Incidentally, these two tubes are rather expensive. Under certain conditions the time limitation may be burdensome to the dermatologist. This is a problem that he must answer for himself, which he can do adequately with a little thought. Before purchasing an unrectified unit, he should obtain from the manufacturer a written statement specifying the minimum number of roentgens which the machine will deliver per minute at a certain distance and for how many continuous minutes it may be operated when delivering the stated output. He should find out also the minimum distance at

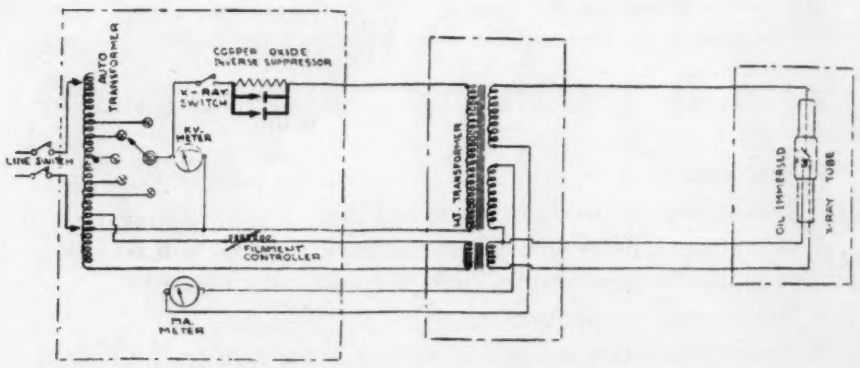


Fig. 2.—Diagram of the circuit of an unrectified unit with inverse suppressor.

which the outfit may be used and the size of the field of exposure at that distance. With this information at hand, the dermatologist or his consulting physicist can readily determine whether the capacity of the equipment will meet his demands.

Shockproof tubes and cables offer, in addition to electrical safety, the advantages of short target-skin distance and ready flexibility. The short target-skin distance is advantageous in that it saves time when extremely heavy doses are to be given. Several machines will operate satisfactorily at as short a distance as 10 cm. and will give an intensity of radiation of as much as 900 r per minute. The increased flexibility of tube housing is especially valuable in treating lesions in the axillas and about the perineum. In our opinion this is a most valuable point. The only disadvantage of the shockproof apparatus is the tendency for the cables to break down from time to time, but the relatively slight cost and inconvenience of replacing a cable are well justified in view of the

obvious benefits derived from its use. Great advances have been made in the past year or so in the construction of these cables, and the number of breakdowns is not nearly as great as it was in the past.

The use of inverse suppressors in the low voltage side of the high tension transformer also greatly decrease the strain on the cables and lessens the chance for electrical breakdown. These suppressors are located in the primary circuit of the high tension transformer and serve to equalize the inverse and useful voltages. Without these units the inverse voltage may be 10 to 20 kilovolts higher than the useful voltage. Thus, on an unrectified machine operating at 85 peak kilovolts the cables and x-ray tubes might be subjected to a strain of as much as 105 peak kilovolts. With the inverse suppressor the maximum strain would be reduced to 85 peak kilovolts, thereby minimizing chances of electrical breakdown.

The early shockproof tubes were constructed with considerable inherent filtration, many of them having the equivalent of 2 mm. of aluminum. This inherent filtration has been gradually decreased by the tube manufacturers until most of the tubes at the present time have the equivalent of about 0.5 mm. of aluminum as an inherent filter. It is the opinion of several dermatologists who have used the 2 mm. filter for several years in the treatment of acne that the clinical results are the same as they were accustomed to getting previously with no filter, provided that the same number of roentgens is administered in each case. Many dermatologists do not take account of the fact that the radiation is at all times filtered through the glass wall of the x-ray tube. In old tubes this envelope varied in thickness from one tube to another —not infrequently by at least as much as the equivalent of 0.5 mm. of aluminum. Consequently the use of a built-in filter of 0.5 mm. of aluminum is not as radical as it might seem at first thought. This much variation in filtration has been present all these years, but the dermatologist usually did not recognize it.

CONCLUSIONS

The increasing use of unrectified x-ray machines by dermatologists is well justified and is associated with the development of better shockproof apparatus and the greater hardiness now obtainable in x-ray tubes with more efficient methods of cooling. The use of inverse suppressors in the primary circuit tends to minimize electrical breakdown.

There is no qualitative difference in the biologic action of x-rays from rectified and from unrectified machines. The effective wavelength and half value layer may be easily determined for either type of apparatus and are the true expression of quality of radiation for any given machine.

The output of unrectified machines (roentgens per minute at a given distance; voltage, and milliamperage) is in general the same as that of rectified machines.

The chief advantages of an unrectified machine are low initial cost and maintenance, diminution in noise and radio interference, easy installation and small space requirement. In many instances it is unnecessary to have a special power line—the machine may be satisfactorily operated from an ordinary 110 volt outlet.

The time limitation for continuous running of unrectified machines is not a handicap in ordinary dermatologic practice, in which the dermatologist is his own operator. This is true because enough time elapses between consultations and in the preparation of each new patient to keep the x-ray tube from becoming overheated.

8 South Michigan Avenue and 826 East Sixty-First Street.

1317 Judson Avenue.

OLD EPIDEMICS OF SYPHILIS

THEODORE ROSENTHAL, M.D.
Director, Bureau of Social Hygiene, Department of Health
NEW YORK

Public health recognition of syphilis as an epidemic disease is of relatively recent origin. The precise epidemiology of syphilis naturally could not be established before the discovery of the spirochete and of the serologic test for syphilis, both of which were made in the early years of the present century.

Medical publications since the return of Columbus' voyagers have, however, described epidemics of disease which in the light of present knowledge are realized to have been epidemics of syphilis.[1] These outbreaks have been given different names according to the geographic localities in which they occurred.

Many of these descriptions were amazingly accurate, not only as to clinical symptoms but in the account of the sequence of infection.

It is interesting and indeed profitable to reflect on epidemics which appeared suddenly in communities which had never before witnessed such diseases and to read of the manner in which infection was transmitted from one person to another. With modern knowledge of the epidemiology of syphilis, this, of course, is a natural and expected course. In the old days, however, these apparent supernatural visitations were attributed to various causes. It may be desirable briefly to review some of the special epidemics and the special names attached to them as they are occasionally encountered in the literature, both medical and popular.

MORAVIAN EPIDEMIC: MORBUS BRUNNO—GALLICUS (1578)

One of the earliest recorded epidemics was that called morbus brunno—gallicus, which broke out in 1578 in Brunn, Moravia. Thomas Jordanus, who described this pestilence, ascribed it to a barber who made scarifications with a dirty razor. Another account, by Geigel, relates that over 180 persons were infected through cupping in a public bath house. The patients were treated with mercury and sudorific substances.

1. Buret, F.: Syphilis in the Middle Ages and in Modern Times, translated by A. H. Ohmann-Dumesnil, Philadelphia, F. A. Davis & Co., 1895, vol. 2. Rayer, P. F. O.: A Theoretical and Practical Treatise on the Diseases of the Skin, edited by J. Bell, Philadelphia, Carey & Hart, 1845.

Thus not only is the modern bathtub a potential source of danger to the public health, but the medieval bathhouse was even more so.

MASSACHUSETTS EPIDEMIC (1646)

In 1646, twenty-six years after the landing of the Mayflower, Gov. John Winthrop of the colony of Massachusetts reported an outbreak of syphilis in Boston. His account, quoted from his journal, reveals an amazing realization of the transmission sequence in the epidemic:

1646 There fell out a loathsome disease at Boston which raised a scandal upon the town and country, though without just cause. One of the town having gone cooper in a ship, on his return, his wife was infected with lues venerea which appeared thus: being delivered of a child, and nothing then appearing, but the midwife, a skillful woman, finding her body as sound as any other, after her delivery, she had a sore breast, whereupon divers neighbors resorting to her, some of them drew her breast, and others suffered their children to draw her, and others let her child suck them, (no such disease being suspected by any) by occasion whereof about 16 persons, men, women and children, were infected, whereby it came at length to be discovered by such in the town as had skill in physic and surgery, but there was not any in the Country who had been practiced in that cure. But (see the good providence of God) at that very season there came by accident a young surgeon out of the West Indies, who had had experience of the right way of the cure of that disease. He took them in hand, and through the Lord's blessing recovered them all in a short time. And it was observed that although many did eat and drink and lodge in bed with those who were infected and had sores, etc.; yet none took it of them, but by copulation or sucking. It was very doubtful how this disease came at first. The magistrates examined the husband and wife, but could find no dishonesty in either, nor any probable occasion how they could take it by any other (and the husband was found to be free of it). So it was concluded by some that the woman was infected by the mixture of so many spirits of men and women as drew her breast (for thence it began). But this is a question to be decided by physicians.

AMBOINA (1718)

In 1718 a peculiar disease was reported by Bontius from the Island of Amboina, one of the Dutch East Indies, and called either Amboina boils or Amboina pustules (*bouton d'Amboin*). The symptoms were the same as those of syphilis, with the difference that the disease could be communicated *sine congressu venereo*. Deep ulcers, caries of the bones and tumors of the limbs, which broke down and discharged gummy matter, were described.

RADESYGE—NORWAY AND SWEDEN (1720)

Endemic syphilis in Norway and Sweden, known as radesyge, or the "bad disorder," is said to have been brought from India to Scandinavia about 1709 by the crew of a Danish ship. Its characteristics were cutaneous eruptions, tubercles of the skin, ulcers, caries of the

bones, alopecia and genital lesions. Most Swedish physicians believed it was syphilis.

Earliest traces in Norway date back to 1720; by the middle of the eighteenth century the disease was widespread, reaching a climax in the last quarter; it was so prevalent on the coast at Bergen and Christiansand that special hospitals had to be provided for patients. Eventually it lost its epidemic character. It appeared in Sweden in 1762, after troops returned from the Seven Years' War; the second importation, in 1790, accompanied Swedish troops returning from Finland. It was still existing in 1885, in Bohuslän, Tjörn, Orust and Lahne.

Radesyge represented a severe form of syphilis complicated with scabies, lupus and other maladies. At one time it was confused with spedalskhed (leprosy); Hebra succeeded in differentiating the two.

DISEASE OF SAINTE EUPHÉMIE—FRANCE (1727)

The disease of Sainte Euphémie was introduced into the community of that name in France by a midwife. Buret stated:

> In the month of May, 1727, a midwife of Sainte Euphémie was attacked, on the forefinger of the right hand, with a pustule,—and soon the body was covered with a universal eruption (*dartre*). This woman, continuing to follow her profession, communicated her disease to more than fifty pregnant women.

Some lost their hair, had angina and communicated the disease to their husbands. A surgeon who was consulted diagnosed "syphilitic herpes," on account of the resemblance and because he did not dare to say "syphilis"—why, it is not apparent, for it would have been much simpler.

PIAN DE NÉRAC (1752)

Raulin described an epidemic disease which seemed to be analogous to scherlievo and facaldine, under the objectionable name of *pian de Nérac:*

> At the end of the month of June 1752, a singular epidemic disease appeared at Nérac; it was a species of lepra or framboesia (pain), similar to that which affects the negroes in the Gulf of Mexico. It spreads among children at the breast; those affected by it begin to fall off; by degrees pustules appear on the face, mouth, neck, buttocks, and thighs. Nurses contract this eruption on the breasts, and it afterwards appears over the whole body. The pustules are generally round, hard, and rather callous; from some of them, a yellowish ichor is discharged; others are covered with a pulverulent crust; these pustules, covering the body, become confluent, and appear to form only a single incrustation; they degenerate into deep ulcers which lay bare the bones, and occasion death; towards the end of December it was calculated that more than forty infants had already been affected with this disease. The treatment that was most successful

was the use of an ointment, made with pure mercury, lard, and camphor, well mixed together. Mercurial frictions were tried upon several women, but mercury without camphor was often ineffectual. Children were cured in a fortnight, but it was necessary to continue the treatment for several days afterwards.

SIBBENS—SCOTLAND (1770)

Sibbens was a troublesome infectious disease prevailing in the southwest part of Scotland. It appeared first as a sore throat with a glandular enlargement and later produced on the skin pustules which ulcerated deeply and also small hard reddish knots which later developed into excrescences resembling raspberries. It is supposed to have been introduced by Cromwell's soldiers and to have been identical with yaws, a disease prevalent in West Africa and carried by Negro slaves to the West Indies. It gradually died out.

According to Gilchrist,[2] sibbens showed itself under several forms. Sometimes inflammation of the velum palati and surrounding parts took place and was accompanied with a kind of white eschar, or a superficial bright red ulcer. At the same time, aphthae or small white spots or eschars often occurred on the velum palati or insides of the cheeks. Often, too, a small excrescence or fleshy growth resembling a raspberry developed, and became covered with a scab. This growth was an almost certain indication of the disease, even when the sore throat did not exist.

Sibbens appeared in some cases on the skin, and under different aspects. Sometimes the whole surface of the body was spotted and clouded with a coppery and dusky red blush. At times a species of tumor similar to furuncles affected the arms, shoulders, face, legs and feet, gave rise to ulcers that perforated the whole thickness of the skin and laid bare the muscles, which it sometimes also corroded.

Finally, the aforementioned soft and spongy raspberry tumors (whence the name of sibbens or sivvens, which is derived from sibbens framboesia) were the last symptoms of the disease; they did not seem to occur in all places alike, for several other forms of the disease were observed—several, indeed, which Gilchrist himself had never seen.

The treatment adopted for sibbens bears the greatest resemblance to that employed for syphilis.

DISEASE OF THE BAY OF SAINT PAUL—CANADA (1776-1780)

Between 1776 and 1780 a disease which has been designated under the names disease of the Bay of Saint Paul, *le mal de chicot, le mal des éboulements* and Ottawa disease appeared in Canada, particularly in the Bay of Saint Paul. According to one observer, it was announced by the appearance of a number of small pustules on the lips, tongue

2. Gilchrist, E.: An Account of a Very Infectious Distemper Prevailing in Many Places, Essays & Obs. Phil. Soc. Edinburgh **3**:154-177, 1771.

and inside of the mouth. These pustules, which resembled small aphthae, advanced rapidly; and children were seen whose tongues were almost entirely destroyed by them. The whitish and puriform matter they contained communicated the infection to those who touched it. Patients were tormented with nocturnal pains in the bones, but these generally subsided when ulcers appeared on the skin and in the mouth; cervical, axillary and inguinal buboes often occurred; at a more advanced stage the body became covered with pruriginous tetter, which soon disappeared. The bones of the nose, palate, cranium, pelvis, thighs, arms and hands became affected with nodes and caries; all the functions became greatly disordered; the senses were disturbed; the patients died a prey to the most acute sufferings. Some persons, however, were so robust that they stood out against this complication of infirmities for many years, dragging on a most miserable life; entire limbs were sometimes known to sphacelate and fall off. This frightful disease spared no one, but seemed to rage with peculiar virulence among children. It was, above all, by the sexual act that it was communicated or transmitted from one person to another.

FACALDINE (1786)

Under the name facaldine has been described a variety of syphilis which is said to have been introduced in 1786 into the village of Facaldo, in the province of Bellune, bordering on the Tyrol, by a female mendicant suffering from venereal itch and ulcers and warts on the vulva. The following characteristics were ascribed to facaldine: A scabious syphilitic eruption which attacked adults and children; ulcers in the throat and nasal fossae; destruction of the nose; serpiginous ulcers which eroded the skin in various directions, and gummy tumors (rare). In adults blennorrhagic discharges took place from, and ulcers occurred on, the genital organs; buboes and several species of excrescences were also frequent. Mercurial medicines were used in treating facaldine.

DITHMARSIAN-HOLSTEIN DISEASE (1789)

The origin of the Dithmarsian-Holstein epidemic of syphilis may be traced to the following episode: A large number of foreign sailors, especially from East Friesland, Netherlands, flocked to the south Dithmarschen for embanking the Crown Prince dyke. If they did not actually bring the disease, they were held responsible for its spread. In 1789 the malady was so prevalent in the marshes and thereabouts that in some villages the whole population was affected; toward the end of the century it appeared elsewhere in Holstein. In 1801 it was noted by the Danish government. By 1806 its diffusion was almost universal, extending finally to Kiel, Germany, on the east coast. There was no noticeable decrease until 1840.

SYPHILOIDS OF LITHUANIA AND COURLAND (1757)

The syphiloids of Lithuania and Courland are another addition to the history of endemics of syphilis. In the Lithuanian division of East Prussia syphilis became epidemic in 1757, after the invasion of Russian troops during the Seven Years' War, and it retained its hold as an endemic disease up to 1820, when the strict enforcement of police sanitary regulations put an end to it.

In Courland the epidemic is said to have broken out in 1800, after the landing of Russian troops on the Dondanga coast.

DISEASE OF FIUME OR SCHERLIEVO

The Fiume epidemic, the origin of which was attributed to 4 sailors who were supposed to have brought it from Turkey, appeared in 1800, in the districts of Scherlievo, Gronemico, Dalmatia and Fiume. It was supposed by others, to have been imported in 1790 from Kukulianova, by a peasant named Kumzut. A short time after his return, his father and mother were affected by it, and afterward propagated it in Scherlievo. Another account of its introduction on the Dalmatian coast holds that a sailor imported it into Draga, a village near Fiume. A "pleasure girl," Margaretta, was the first to be infected; hence, the disease was sometimes called margaritizza.

The disease usually commenced with lassitude of the limbs and pains in the bones of the arms, thighs and spine, which increased during the night; the voice became hoarse, and deglutition difficult; the face was flushed; the velum palati, the uvula, the tonsils and sometimes the pharynx and larynx were red. Ulcers, which in some cases evolved with great rapidity, covered the uvula, the tonsils, the velum palati and the surface of the cheeks and lips; caries affected the bones of the nose. The pustules were of a coppery color, round and of varied extent. They most frequently appeared on the forehead and scalp, but they were also seen on the inner surfaces of the thighs, legs and arms and about the anus and genital organs.

CRACOW EPIDEMIC (1805)

Surgeon Johann Nepomuk Rust (1775-1840) frequently observed that syphilis was transmitted through the ritual of circumcision. The description in his book [3] is in brief as follows:

> In the year 1805, several male infants in the Jewish quarter of Cracow, were affected with swollen genitals. The disease became widespread; nearly every newborn Jewish boy had chancres and several who were neglected medically, were unmistakeably syphilitic. When I observed that always only the newborn males were thus infected, and often a few days after Circumcision, I requested to be present at the next ritual. I then saw that a man especially assigned to this

3. Rust, J. M.: Helkologie, Vienna, Camesina, 1811.

performance, drew the blood with his lips after the operation. Consequently I examined this man and found that the entire cavity of his mouth and jaws was infected with venereal ulcers.

DISEASE OF THE DISTRICT OF CHAVANNE (1816)

An epidemic of a disease presenting classic phenomena of syphilis appeared in the Chavanne district of France in 1816, probably as an aftermath of the events of 1815. It was said that Austrian troops had brought it.

A man named Pierre François Goudey, 28 years of age, was the first person attacked. The first symptoms were general weakness and disinclination to work, then pains in the limbs, which lasted about two months; afterward there were inflammatory and aphthous swellings of the lips and the inside of the mouth for nine months; at the same time inflammation occurred in the posterior fauces, and extinction of the voice supervened, lasting for three months; an inflammatory disease also appeared on the scrotum, which the patient attributed to rubbing by his drawers, made of coarse new linen cloth.

Goudey communicated the disease with which he suffered to his 3 young children, all of whom suffered from the swelled and aphthous state of the lips and only 1 from the inflammatory symptoms of the throat and the hoarseness. Goudey had been made prisoner and detained for three days by a troop of Austrians at Montbelard at the time of the second invasion, and he stated that he contracted the disease by drinking out of the same glass immediately after a soldier of that nation, who, he said, had the disease on the lips. It was not until some time after his return home that Goudey felt the first symptoms of his malady. Elizabeth Goudey, 14 years of age, caught the infection from the children of the aforementioned Goudey, her relatives, after eating with them; she experienced pain in the limbs, swelling of the lips, inflammation of the throat and loss of voice. Her brother, François Goudey, about 15, contracted the disease some time after his sister did and experienced the same symptoms, plus ophthalmia, which lasted several months; the eyelids, indeed, remained slightly injected and the eyes watery. The wife of Jean Baptiste Goudey expressed the belief that she had caught the disease from Elizabeth Goudey, from being so frequently in the house and going often there to her meals. The disease showed itself in her by intense pains in the limbs. She had had a general pustular eruption, though the head was the part most particularly affected; marks of this eruption remained, in the shape of spots of a livid red. Her lips were not inflamed, but she had aphthae on the tongue and inflammation of the throat, of which, as well as the hoarseness, she continued to complain. The husband of this woman contracted the

disease six months after her; he suffered from pains in the limbs for only a fortnight; his throat was in a high state of inflammation, and this was accompanied with almost complete extinction of the voice.

JUTLAND SYPHILOID (1817)

The origin of Jutland syphiloid has been traced to the importation into Denmark of syphilis by Russian sailors, or more probably by troops from Sweden and Norway in the middle of the eighteenth century. It appears to have been confined as an endemic mostly to North Jutland. In 1817 it came to the attention of the Danish government. A report made by von Deurs showed that this syphiloid was in all respects identical with sibbens and radesyge.

CAPISTRELLO (1859)

In 1859, according to Hirsch,[4]

> . . . a woman of the village, located in one of the Italian Provinces, took to nurse a strange child suffering from congenital syphilis, and became infected by it. Not knowing the malady, and giving no heed to it in her family intercourse, she soon gave the disease to those about her; from these it was conveyed to others in the village, and so extensively did it spread that after a lapse of eight years (down to October 1867, when the attention of the authorities was first drawn to it), during which we hear nothing either of diagnosis or treatment, more than 300 persons, men and women, children and the aged, were infected with syphilis out of some 3000 who formed the population of the locality.

4. Hirsch, A.: A Handbook of Geographical and Historical Pathology, translated by C. Creighton, London, New Sydenham Society, 1885, vol. 2.

KERATODERMA CLIMACTERICUM

(HAXTHAUSEN'S DISEASE)

LAWRENCE C. GOLDBERG, M.D.
CINCINNATI

It has been said that "skin diseases mirror the system," which holds true in various forms of keratoderma associated with disturbances of the endocrine system. Mussio Fournier [1] described cases in which keratoses of the palms and soles cleared after treatment with desiccated thyroid. Cervino and his associates [2] reported keratoderma of the palms and soles in a girl aged 15 and a woman aged 41 who had basal metabolic rates of —24 and —41 per cent, respectively, and improved greatly under thyroid medication, so that the keratoses became detached in lamellas and ultimately disappeared. Haxthausen [3] described keratoses of the palms and soles in 10 women in association with the menopause and accompanied with various signs and symptoms, of which obesity, hypertension and arthritis were the most frequent. The hyperkeratotic process appears in its earliest stages as a discrete sharply defined round or oval lesion of regular form. The horny layer is often frayed and occasionally crossed by superficial fissures, and in the early stages there are no miliary vesicles or other evidences of eczema. The skin beyond the part actually affected is in many cases dry and shows diffuse thickening of the horny layer with accentuation of the natural folds. The keratotic elements are localized mainly to the part most exposed to pressure and noted in symmetric distribution.

Barber,[4] in commenting on Haxthausen's paper, stated that he believed Haxthausen's description was of the same disease he had presented before societies. The characteristics in his cases were: (1) erythema of the palms and soles, which tended to invade the

1. Mussio Fournier, J. C.: Kératodermie plantaire et palmaire chez une hypothyroïdienne: La guérison par la thyroïdine, Bull. et mém. Soc. méd. d. hôp. de Paris **48**:1236 (July 18) 1932.

2. Cervino, J. M.; Bertolini, A., and Larrosa Helguera, R. A.: Keratodermias of the Hands and Feet and Thyroid Deficiency, Endocrinology **22**:615 (May) 1938.

3. Haxthausen, H.: Keratoderma Climactericum, Brit. J. Dermat. **46**:161 (April) 1934.

4. Barber, H. W.: Symmetrical Hyperkeratosis of the Palms and Soles, Brit. J. Dermat. **46**:254 (May) 1934.

lateral surfaces of the hands and feet, (2) hyperkeratosis corresponding exactly to sites of maximum pressure and friction, (3) formation of deep painful cracks in the hyperkeratotic areas and (4) subjective sensations of burning and itching in the palms and soles.

Neither in Haxthausen's cases nor in the case here reported was there any erythema, nor did the patients complain of itching or burning. Barber's patients were 3 men and 3 women; in 4 of these the uric acid level of the blood was raised, leading him to believe that the primary factor was a metabolic disorder and that it should respond to dietary restrictions. Haxthausen reported discouraging results from treatment with a thyroid preparation and various ovarian preparations, and stated he did not produce a definite cure with these medicaments in any case.

Since I have not found any previous report on this unusual form of keratoderma in the American literature and because the results of treatment were so encouraging, the following case is reported:

REPORT OF A CASE

M. D., a white married woman aged 49, was first seen on July 2, 1938, having been referred to me by Dr. Meyer Zeligs because of "painful calluses" on both soles. She had previously consulted her physician because of nervousness, occasional dizziness, headache and generalized weakness.

The patient stated that since panhysterectomy had been done, ten years before, she had gradually become weak and nervous and had stopped menstruating. During the past three or four years she had noticed the development of extremely painful "calluses" on both soles, which had gradually extended over the entire plantar surface and finally incapacitated her to such an extent that she had great pain when walking. She also complained of rheumatic pains in her hands and knees. There was no history of the ingestion of arsenic and no similar disturbance in any member of her family, including her brothers and sisters.

Physical Examination.—The patient was small and obese but not acutely ill, although she complained bitterly of pain when walking. Her height was 5 feet 3 inches (160 cm.), and she weighed 165 pounds (75 Kg.). Except for her blood pressure, which was 155 systolic and 95 diastolic, physical examination gave essentially negative results. The present description will be confined to the patient's cutaneous lesions.

On the palms were definite plaquelike hyperkeratoses, confined to the hypothenar eminence. On the soles were extensive hyperkeratotic plaques, which formed deep sulci and extended up to but did not involve the interdigital spaces. They were present on the lateral surfaces of the insteps and the backs of the heels, but did not involve the achilles tendon. In some areas, particularly about the heel, the keratoses had a granular appearance and when removed left a raw, bleeding surface behind. There were no miliary vesicles and no weeping areas, and the patient did not complain of itching or burning, but only of pain on walking.

Laboratory Tests.—No fungi were demonstrated, microscopically and by culture. The Wassermann reaction of the blood was negative. The uric acid level was normal.

Treatment.—The patient was given estrone (theelin) in oil, 2,000 units intramuscularly twice a week, for two months. She also received treatment with unfiltered roentgen rays, 100 roentgens, to the soles at weekly intervals for seven weeks.

On August 13 she was discharged and her feet were perfectly normal. In the six months which has elapsed since that time, there has been no recurrence of the keratoses.

A histologic examination of this dermatosis was not possible, as a biopsy specimen was not available; so the description which follows is a condensation of Haxthausen's histologic observations: The lesion examined was a small pea-sized papule removed from the base of the thenar eminence, which showed considerable hyperkeratosis with marked parakeratosis occurring in circumscribed patches, resembling that seen in psoriasis. There was no acanthosis, nor were any microabscesses or vascular formations of the deeper lying cells seen. The corium showed only a small amount of perivascular round cell infiltration.

In the differential diagnosis of keratoderma climactericum one should consider particularly a hyperkeratotic fungous infection, keratoderma palmare et plantare of the hereditary and the acquired form, psoriasis, mal de Meleda and all other forms of keratosis involving the palms and soles.

SUMMARY

A case is reported in which keratoderma climactericum suggested itself not because of the peculiar appearance of the keratosis but because of the association of the lesions with the menopause and the general signs and symptoms of obesity, arterial hypertension and arthritis. This form of keratoderma is not associated with any erythema or with subjective sensations of burning and itching. Biweekly injections of estrone (theelin) in oil (2,000 units) and superficial roentgen therapy brought about a complete cure.

623 Doctors Building.

THIRD GENERATION SYPHILIS

REVIEW OF THE LITERATURE AND REPORT OF A CASE

JAMES A. BRUSSEL, M.D.

BRENTWOOD, N. Y.

Congenital syphilis is always an interesting clinical entity, not only because of its medical significance but for its economic and sociologic implications. Contemporary comment deplores the unreliability and paucity of figures on its incidence. How much more confusing and rare, therefore, are statistics on syphilis transmitted to the third generation! Consequently, the reporting of cases should continue if the mechanism of transmission is to be understood, while, simultaneously, the hapless victims of such a heritage must command one's sympathy and desire for vigorous and early therapy.

As a matter of historical interest, it is not unusual to find older textbooks differentiating "congenital syphilis" and "heredosyphilis." Stokes,[1] for instance, described the latter as a misnomer but a convenient term to cover that type of infection which the child contracts via the placenta and the maternal and the fetal blood stream. Recognizing that "congenital syphilis" and "heredosyphilis had been employed interchangeably, Stokes confined the former term to that syphilitic disease which follows infection of the fetus in passing through the birth canal. However, it is obvious that such infection is rare when it is considered that Stokes described congenital syphilis as an acquired type that the child may easily survive, while implying that heredosyphilis overwhelms the infant with spirochetes whose devastation he outlives only by special resistance or by special protection.

Arcangeli [2] considered the question from another angle. He divided the pathologic phenomena of congenital syphilis into two groups: those due to the transmission of the virus, which he called microbic hereditary syphilis, and those due to the hereditary transmission of a dystrophy dependent on the syphilis, which he called dystrophic hereditary syphilis. Evidently, hereditary dystrophy enters into consideration only in congenital syphilis from the second generation on; the pathologic phe-

---

From the Female Reception Service of the Pilgrim State Hospital.

1. Stokes, J. H.: Modern Clinical Syphilology, ed. 2, Philadelphia, W. B. Saunders Company, 1934.

2. Arcangeli, U.: Introduzione alla clinica della sifilide ereditaria nelle varie età della vita e nelle successive generazioni, Riv. osp. **28**:237 (May) 1938.

nomena of the hereditary dystrophy will be of syphilitic origin, but not of syphilitic character, and therefore are not amenable to antisyphilitic treatment. These observations are interesting but cannot be proved. Arcangeli further stated that microbic hereditary syphilis can be transmitted for at least four generations unless the series is interrupted by treatment or intercurrent diseases capable of damaging the syphilitic virus. However, the literature fails to reveal such lengthy transmission. Accordingly, in congenital syphilis from the second generation on, there may be phenomena due to dystrophic congenital syphilis together with phenomena due to microbic hereditary syphilis. In other words, there may be cases of mixed hereditary dystrophy and microbic congenital syphilis. This may explain why not all the phenomena observed in hereditary syphilis of the second and the third generation are corrected by antisyphilitic therapy.

Von Zumbusch [3] stated that his experience had been that marks of degeneration found in persons with congenital syphilis are not passed on to the next generation. Hutchinson teeth, hydrocephalus and other degenerative symptoms are not found. He added that the serologic reaction is positive frequently up to the age of 20 in patients with congenital syphilis, and it completely resists therapy, becoming negative later even without treatment.

I frankly concede that reluctance to report congenital syphilis beyond the second generation is due to the lack of positive evidence that the disease is truly passed on from one generation to the next. Whether or not it is believed that the disease is to be overcome in time and never become a familial characteristic, cases of syphilis thought to have survived into the third generation have been reported. Authentic or not, such rare cases do not alter the general thesis that the disease must be recognized and treated at the earliest possible moment.

Clark [4] said that third generation syphilis is extremely rare. "The rub comes in the establishing of the prenatal as distinguished from the possibly acquired syphilis of the second generation mother." Various authors have prescribed dictums to be followed in making this unusual diagnosis. For instance, Higoumenakis [5] declared that absolute hereditary syphilis of the second generation must present sure signs of syphilis or more rarely symptoms of virulent syphilis or a positive Wassermann reaction of the blood and absence of a history of contracting the disease. A parent must have been affected by hereditary

3. von Zumbusch, L.: Venereal Diseases and Marriage Consent, Int. Clin. **2**:62 (June) 1928.

4. Clark, J. C.: Third Generation Syphilis, J. A. M. A. **109**:1038 (Sept. 25) 1937.

5. Higoumenakis, G. C.: The Virulent Form of Hereditary Syphilis of Second Generation, Indian J. Ven. Dis. **4**:65-77 (June) 1938.

syphilis without evidence of having contracted it; nor must the mother have been affected by acquired syphilis. The grandfather, or at least the grandmother alone, must have been affected by it. Higoumenakis also pointed out that hereditary syphilis of the second generation is usually silent. In its virulent form the spirochete becomes less virulent in passing on from the first to the second set of progenitors.

The pathetic part of congenital syphilis is that it is usually discovered "backward." That is, a child brought to a physician for some minor ailment furnishes the first clue. Routine examination reveals the presence of syphilis, and this suggests examination of the parents, the finding of infection in whom usually leads to serologic studies of the grandparents. These were the conditions in the case to be reported.

Statistics are meager on congenital syphilis extending beyond the second generation. In 1904 Fournier reported the virulent form. Milan in 1934 cited a case, as did Schlumberge. Higoumenakis later cited 4 additional cases, making a total of 15 in the literature. I am reporting another. Yet there must be more frequent occurrences if Whipple and Dunham's [6] estimation of second generation syphilis is correct. They cited figures to the effect that of 683,000 persons with syphilis who are constantly under observation in the United States, at least 60,000 (over 11 per cent) are suffering from an infection transmitted by the parent. They expressed the belief too that the generally accepted mode of transmission is from the syphilitic mother through the placenta, even though the mother may show no clinical manifestations of the disease.

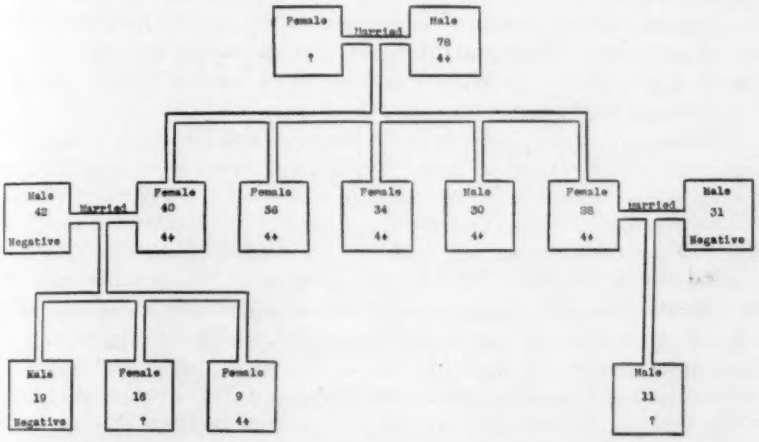
Whipple and Dunham stated that the diagnosis of congenital syphilis may be made only by a correlation of several factors: (1) demonstration of the disease in the parents, (2) examination of the placenta and cord, (3) pathologic examination of the stillborn infant, (4) clinical examination of the living infant, (5) serologic tests of the living infant and (6) roentgen examinations of the bones of the living infant. Recently, it was stated by Rössle [7] that familial syphilis presents the same variegated and checkered picture as extrafamilial syphilis, thus bearing out a parallel statement made by Stokes many years ago.

While the so-called laws of Colles and Profeta have generally been disproved, it remains a clinical curiosity to see presumably healthy children of syphilitic mothers or healthy siblings of a congenitally diseased child. This situation was present in the case to be reported. Here were 3 children, of whom the youngest was congenitally syphilitic

6. Whipple, D. V., and Dunham, E. C.: Congenital Syphilis: I. Incidence, Transmission, and Diagnosis, J. Pediat. **12**:386 (March) 1938.

7. Rössle, R., cited in International Medical Week, Foreign Letters (Switzerland), J. A. M. A. **109**:1827 (Nov. 27) 1937.

and the oldest apparently unaffected while the second sibling refused serologic examination but was clinically free of syphilitic symptoms. Stokes has offered a logical explanation for such a family. Maternal spirochetemia, which probably precedes placental infection of the child, can hardly be a continuous phenomenon, and it is easily imaginable that with a suppressed and thoroughly latent infection the mother may go for months or even years without the lodgment of a single spirochete from her blood stream in the placenta. Likewise, the prolonged latency of a uterine syphilitic infection in the child has been too well demonstrated today to allow further doubt. Infants who appear well and perhaps respond to early Wassermann tests negatively may later in life, with the advent of diminished resistance, injury, puberty and the like, show unquestionable and active signs of syphilis. Consequently,



Genealogic chart, showing sex, age and Wassermann reaction of members of the family for three generations.

what constitutes a healthy child of a syphilitic mother is to be decided not weeks but perhaps years after the initial observation.

Therefore, I repeat, in the light of the rigid standards for making the diagnosis of third generation syphilis, I believe the following case to be one of true syphilis transmitted beyond the second generation. When certain features appeared doubtful, they have, nevertheless, been included with the positive evidence.

REPORT OF CASE

This series, as stated before, was discovered "backward"; i. e., the third generation was found first to be syphilitic. The child, a girl aged 8 years, was brought to her family physician because of "swollen glands." Physical examination revealed cervical adenopathy, with several sinuses discharging purulent matter, perforation

of the soft palate, "snuffles" and interstitial keratitis on the right. Emotionally she was unruly, restless and generally uncooperative, so that at school she was regarded as a "problem child." The Wassermann reaction of the blood was 4 plus; the spinal fluid was entirely normal. The next eldest child, a girl, refused serologic examination, but the Wassermann reaction of the eldest, a youth aged 19, was negative, and he presented no clinical signs of syphilis.

The mother on examination presented signs of syphilitic aortitis with hypertensive cardiovascular disease. In the light of the subsequent history, this is regarded as the result of congenital syphilis. At this point I may mention that the child after five months of intensive therapy presented healed adenopathy; her keratitis had subsided, and she was no longer irritable and did excellent work in school. The mother has been receiving treatment for the past nine months, with no change in the cardiovascular picture. The father of the child, fortunately for the purpose of accuracy of this report, has been in a type of occupation where a regular check-up of his blood is required. His Wassermann reaction has remained negative, as it was prior to marriage. His wife, who is frank and open about the most personal matters, steadfastly maintains that she did not have prenuptial or extramarital sexual intercourse. It is felt that she, along with her 4 siblings, inherited her infection. These facts are also to be regarded in the light of her early marriage, at the age of 19.

This woman's younger sister is single but states that she is not a virgin. She came under observation when brought to Bellevue Hospital in New York city, after an attempt at suicide at the height of a depressive attack, from which she has since recovered. Physical examination showed no abnormality, but the Wassermann reaction of the blood was 4 plus. Examination of the spinal fluid gave completely negative results. She, too, continues under adequate treatment. The next younger sibling is a woman aged 34, who is hospitalized at this time because of mental symptoms and physical signs characteristic of dementia paralytica. The Wassermann reaction of the blood and of the spinal fluid were both 4 plus. The relatives know nothing of her sexual history, and the patient is out of contact. At this time she is completing her course of malaria therapy. The next sibling in this interesting second generation is a man, who furnished a strong piece of evidence so far as his and his sisters' inheritance of syphilis is concerned. At the age of 14 he was overactive, irritable, antagonistic and assaultive, and after examination the family was told the boy "was suffering from a blood disease." He ran away, is supposed to have made an unfortunate marriage later, which terminated in separation, and was finally hospitalized because of a mental illness characterized by manic excitement, hyperactivity and overproduction. The Wassermann reaction of his blood was 4 plus. Examination of the spinal fluid was not made. The youngest sibling, a woman of 28, was married to a man with a negative Wassermann reaction of the blood and no clinical signs of syphilis. This woman, however, presented another important piece of evidence: She had been "deaf since infancy" and was raised in an orphanage until she was 16. At that time she left the institution and promptly married. She had since been hospitalized because of a manic-depressive psychosis. The Wassermann reaction of her blood was 4 plus, but examination of the spinal fluid gave negative results. This couple had 1 child who, although no serologic data are available, had been "sickly since birth" and at the age of 4½ years was operated on for "mastoid trouble." In this series, then, is the variegated appearance of congenital syphilis.

The picture became more ironic when the first generation—the grandparents—were considered. The mother was dead, and the daughters stated that they were told by "the doctor that death was due to a clot in the brain from blood disease." The husband of this woman (the grandfather of the series) was living at the age of 78, with a 4 plus Wassermann reaction of the blood. He was apparently in "good" health, despite his untreated disease.

Recalling, as pointed out early in the paper, that inherited syphilis may demonstrate a variegated and almost illogical picture and measuring the case presented by the yardsticks of Higoumenakis and Whipple and Dunham, I feel that the offspring of the third generation described is a victim of third generation syphilis.

SUMMARY

1. Syphilis of the third generation is considered.
2. The literature is surveyed and discussed.
3. A case of third generation syphilis is presented.

RELATION BETWEEN PIGMENTATION AND GROWTH OF HAIR

PIGMENTARY EFFECTS OF ANTHRALIN (DIHYDROXYANTHRANOL) IN TWO CASES OF ALOPECIA AREATA

M. H. GOODMAN, M.D.
Instructor in Dermatology, Johns Hopkins University School of Medicine
BALTIMORE

Dihydroxyanthranol-1, 8, under the trade name cignolin, was introduced into dermatology in 1916 by Galewsky [1] and Unna,[2] who stressed its value as a substitute for chrysarobin in the treatment of psoriasis. Beerman and his collaborators,[3] in reporting on this chemical, known in America by the name anthralin, in 1935, discussed its properties and its successful employment in the treatment of a number of dermatoses and especially emphasized its use in low concentrations (from 0.1 to 1 per cent) with relatively little irritating effect even when applied to the scalp or face. They referred to its effectiveness for alopecia areata and stated that in some cases they obtained a better effect by combining its use with ultraviolet irradiation. In the discussion of this report it was brought out that the beneficial effects on certain cutaneous conditions of chrysarobin, dihydroxyanthranol and anthrasol are, as in the case of coal tar, attributable to their strong reducing powers. The dermatitis-provoking properties of anthralin and its ability to produce pigmentation of the skin were also discussed.

The pigmentary reaction obtained in the following 2 cases of alopecia areata was interesting from the standpoint of the probable relation between pigment formation and the growth of hair.

From the Department of Dermatology, Johns Hopkins Hospital.

1. Galewsky, E.: (*a*) Ueber Cignolin, ein Ersatzpräparat des Chrysarobins, Dermat. Wchnschr. **62**:113, 1916; (*b*) Cignolin, ein synthetisches deutsches Chrysarobin, und Laneps, eine neue Salbengrundlage, Deutsche med. Wchnschr. **43**: 238, 1917.

2. Unna, P. G.: (*a*) Cignolin als Heilmittel der Psoriasis, Dermat. Wchnschr. **62**:116, 150 and 175, 1916; (*b*) Ueber die Einwirkung von Cignolininjektionen auf das Hautgewebe, ibid. **69**:811, 1919; (*c*) Pyrogallol, Cignolin und der antipsoriatische Effekt, Wien. klin. Wchnschr. **35**:387, 1922.

3. Beerman, H.; Kulchar, G. V.; Pillsbury, D. M., and Stokes, J. H.: Dioxyanthranol 1-8 as a Substitute for Chrysarobin, J. A. M. A. **104**:26 (Jan. 5) 1935.

REPORT OF CASES

CASE 1.—Mrs. W. S. W., an American-born white woman, complained of a general loss of hair of seven years' duration. At the onset the condition was treated by ultraviolet irradiation, but this was suspended after twelve applications because of a severe reaction. A general physical examination at that time showed no abnormality except that the patient was considered to be nervous. Rest in bed was advised. For four years she had been under treatment by a "scalp therapist" with ultraviolet irradiation, massage and proprietary local applications. No appreciable improvement resulted from this treatment. When I first saw her, on April 27, 1936, general physical examination showed no essential abnormality. The menstrual periods were regular and lasted four or five days, but there was occasional dysmenorrhea. The blood count and blood pressure were within normal limits. The Wassermann reaction of the blood was negative and examinations of the urine showed nothing abnormal. The integument was dark and thin and perspired normally; aside from four small tufts of black hair at the vertex of the scalp and a few eyelashes on the upper right lid, there was total alopecia of the entire body.

From time to time during treatment the patient suffered from "nervous spells," headaches and insomnia. A recurrent neurodermatitis (lichen simplex chronicus) of the elbows, which had appeared concurrently with the alopecia seven years before, was controlled with sedatives and antipruritic lotions and ointments.

Local treatment was instituted with ointments containing small amounts of sulfur, salicylic acid and coal tar in combination and varying percentages of anthralin. The patient applied this to the scalp once daily and occasionally wiped her scalp lightly with xylene. Anthralin in an ointment with other chemicals as mentioned or alone in concentration ranging from 0.125 to 0.5 per cent as tolerance developed was applied for several months. A mild dermatitis of the scalp appeared soon after the commencement of treatment, and within one month there was decided pigmentation, which persisted with little or no accompanying inflammatory reaction. Ultraviolet radiation in suberythema doses was also administered once or twice a week with some irregularity. There was evidence of growth of hair within six weeks after the commencement of treatment. In a dozen or more areas varying in size from that of a nickel to that of a quarter on the occipital and parietal regions there was a good growth of hair in tufts which had attained substantial length and color six months later (October 1936). There was also a diffuse growth of lanugo over the frontal region.

From August 1936 to January 1937, between menstrual periods, the patient received estrogen (progynon), 2 tablets containing 225 international units (equivalent to 45 rat units) daily. Beginning in January 1937 she was given twelve injections (intramuscularly twice weekly) of 1 cc. of anterior pituitary extract (each cubic centimeter the equivalent of 1⅛ grains [0.07 Gm.] of fresh anterior lobe of the pituitary body). This medication apparently produced no favorable effect on the growth of hair over and above that which would have resulted from the local therapy.

By the first of June 1937 there had been a progressive but slow growth of long tufts of hair over the scalp except in the frontal region, where lanugo was present. When the patient was seen on June 25, a remarkable change was noted. All the hair had fallen out, and there was complete depigmentation of the scalp. The integument of the scalp had evidently been exhausted of its pigment-forming power in a vitiligo-like manner, because during a further three months' observation no pigmentary response could be elicited with anthralin or ultraviolet radiation, and, incidentally, there was no regrowth of hair.

CASE 2.—Mrs. E. G., a white American woman aged 28, six months after marriage in January 1937 noticed a fall of hair in spots over the front and back of her scalp. She was in good general health except for nervousness, which started while she was under a considerable strain in the year prior to her marriage and was aggravated by the shock of her father-in-law's death by drowning. From the onset until I first saw her, in November 1937, she had been treated by a "scalp therapist," who used massage, application of chemicals and ultraviolet irradiation with no appreciable effects.

Her past history showed that ten years before she had had an appendectomy and six years ago her gallbladder had been drained. Recently there had been no significant abdominal symptoms. On general examination no evidence of organic disease was discovered. The Wassermann reaction of the blood was negative and examination of the urine showed no abnormality. The blood cell count, hemoglobin concentration, sedimentation rate and icteric index were normal. Gastric analysis and examination of the stool gave negative results. The nonprotein nitrogen content of the blood was 24 mg. per hundred cubic centimeters and the sugar content during fasting 87 mg. per hundred cubic centimeters. The basal metabolic rate was +20 per cent.

The alopecia areata was limited to the scalp. There were a palm-sized area of complete baldness over the left temporofrontal area and a slightly smaller area in the corresponding position on the right side. At the vertex of the scalp there was a quarter-sized area of alopecia, and back of this and extending over the central occipital region there were two adjacent areas roughly the size of a silver dollar. The intact hair of brunet type was of good length and served well to disguise the presence of the alopecia. All the bald spots were sharply circumscribed and smooth except for a few marginal lanugo hairs in the areas in front. The bald integument conformed in every respect with the general cutaneous surface, which was dark. There was no seborrhea, and perspiration was normal.

Because of the good effect on growth of hair obtained in case 1, anthralin was used in this case also, in ointments combined with salicylic acid, with resorcinol, with sulfur and with coal tar and alone in concentrations of 0.125 to 0.5 per cent. A mild reaction developed quickly, and the skin took on a dark "sunburn tan" appearance. After three months the coloring was blackish brown, and there was a substantial growth of hair, especially in the frontal bald regions. This new hair was not lanugo alone, but much of it was fully developed. The growth was both diffuse and in the form of tufts, which developed a brunet color and a length of 1 inch (2.5 cm.) or more. For short periods at various intervals the patient took tablets of estrogen (each 225 international units) twice daily for ten days prior to the menstrual periods. This was done because her periods lasted but two and one-half days. Later, compound solution of iodine U. S. P. was administered in a dose of 5 drops twice per day. She was directed to rest in bed as much as possible. Such treatment was continued for a month on two different occasions. No special benefit apparently accrued, so far as the scalp was concerned. Ultraviolet radiation to the scalp was given once or twice weekly at intervals, and for short periods a daily application of xylene to the scalp was prescribed. From the date of the initiation of treatment until June 1, 1938, one daily application of the anthralin ointment was made, with only occasional omission because of symptoms of irritation. During the last week of June a sudden change took place. As in the first case, the scalp became completely depigmented, and the new hair also completely disappeared. Attempts to elicit a pigmentary reaction with anthralin and ultraviolet radiation failed. For about five months thereafter

the involved areas showed no change under an indifferent form of local stimulating therapy. In December 1938 the large right frontal area and an occipital area of baldness began to show some darkening from the hitherto total vitiligo-like whiteness toward a restoration to the normal brunet complexion. Suberythema doses of ultraviolet radiation were then given twice weekly. An obvious tanning effect of all areas was noted after one month. By the middle of February 1939 many new hairs appeared in the frontal and occipital areas and at the time of writing (April 1939) some of the hairs are attaining good length.

COMMENT

In the 2 patients regrowth of hair occurred in conjunction with increasing pigmentary reaction produced by anthralin, and the fall of hair coincided with the sudden depigmentation obviously effected by the exhaustion of the pigment-producing power of the integument of the scalp. This incident calls to mind the opinion of Bruno Bloch with regard to vitiligo, which he called an exhaustion dermatosis in which the local oxidase enzyme is used up on account of some unknown stimulant, probably referable to the endocrine-sympathetic system. Of further interest in this connection is the subject of the occurrence of alopecia areata and vitiligo in the same patient, an observation first made by Anderson [4] in 1879. The same author [5] later recorded such a case in which the vitiligo involved sites previously affected by alopecia areata. Senator [6] and later Feulard [7] each observed a case of similar involvement, but they expressed the belief that there was no special significance in the association of the two diseases in the same patient. Feulard's patient was a 12 year old girl with vitiligo, in whom alopecia areata developed. The vitiligo had involved the scalp in the form of numerous tiny islands in which the hair was white. When the hair regrew rapidly under simple treatment, these islands again showed the white hair of the original vitiliginous character and not regrown hair of the type common after alopecia areata. Crocker [8] contended that since vitiligo itself is a rare disease its occurrence in 1 per cent of cases of alopecia areata (according to his observations) is sufficiently frequent to justify considering these diseases related on an etiologic basis of trophoneurosis.

4. Anderson, T. M'C.: On a Case of Addison's Disease Improving Under Treatment and on the Relationship Between Addison's Disease, Vitiligo and Alopecia Areata, Glasgow M. J. **11**:14, 1879.

5. Anderson, T. M'C.: Alopecia Areata, in A Treatise on Diseases of the Skin, Philadelphia, P. Blakiston's Son & Co., 1887, p. 61.

6. Senator, H.: Combination von Alopecia areata und Vitiligo, Charité-Ann. **14**:341, 1889.

7. Feulard, H.: (*a*) Pelade décalvante et vitiligo, Ann. de dermat et syph. **3**:842, 1892; (*b*) Pelade décalvante et vitiligo: Guérison de la pelade, ibid. **4**:31, 1893; (*c*) Pelade et vitiligo, ibid. **4**:1311, 1893.

8. Crocker, H. R.: Alopecia Areata, in Diseases of the Skin, Philadelphia, P. Blakiston's Son & Co., 1903, p. 1209.

Ayres [9] reported the case of a woman with long-standing alopecia areata in whom symptoms of hyperthyroidism and shortly thereafter vitiligo developed. Lévy-Franckel and Juster [10] expressed the belief that the sympathetic nervous system is disturbed in the presence of alopecia areata because of its observed association with vitiligo. Barber [11] stressed the frequency of concurrence of the two diseases and reported a case in which they appeared concomitantly and in which psychic (shock) stimuli apparently lay at the base of the sympathetic disturbance leading to them. Brown [12] favored an etiologic relation based on a disturbance in the endocrine-sympathetic system and mentioned a case of alopecia areata with vitiligo of the skin of the scalp. Roxburgh [13] found vitiligo in only 1 of a series of 100 cases of alopecia areata and expressed the belief that the two diseases are not related.

The livid or pale pinkish appearance of the patches of alopecia areata is probably attributable to the absence of perifollicular pigment but in no sense to any associated vitiliginous disturbance in pigment formation. This is brought out by the fact that such bald areas can be uniformly tanned by exposures to ultraviolet rays.

Although the evidence in the literature suggests, though remotely, a possible etiologic relation between alopecia areata and vitiligo, there is nothing in the accumulated data to indicate that in any locally involved area of a patient suffering from both diseases the process of pigment exhaustion can be coupled with the fall of hair. On the contrary, the evidence would seem to permit the conclusion that pigment formation and growth of hair are based on distinct mechanisms which never merge. For these reasons the course of events in the 2 cases reported here are of unique interest, in that they seem to indicate that pigment formation and exhaustion may under certain circumstances influence respectively the growth and loss of hair. It is suggestive that anthralin by its strong reducing properties in pigmenting the skin of the scalp of 2 women with alopecia areata produced an excellent growth of hair. On the other hand, with persistence in the use of this chemical there was sudden evidence of exhaustion of pigment formation, and coincidentally with this phenomenon all the regrown hair fell out. It must be noted that

9. Ayres, S., Jr.: Vitiligo and Alopecia Areata Associated with Severe Hyperthyroidism: Report of a Case, Arch. Dermat. & Syph. **8**:502 (Oct.) 1923.

10. Lévy-Franckel, A., and Juster, E.: Recherches sur le mécanisme physiopathologique de la pelade, Ann. de dermat. et syph. **9**:285, 1928.

11. Barber, H. W.: Lettsomian Lectures on the Relationship of Dermatology to Other Branches of Medicine, Lancet **2**:591, 1929.

12. Brown, W. H.: The Aetiology of Alopecia Areata and Its Relationship to Vitiligo and Possibly Sclerodermia, Brit. J. Dermat. **41**:299, 1929.

13. Roxburgh, A. C.: The Aetiology of Alopecia Areata and Its Relation to Vitiligo and Sclerodermia, Brit. J. Dermat. **41**:351, 1929.

in case 2 with the fall of the regrown hair there occurred in regions uninvolved by the alopecia areata some fall of hair, both diffusely and focally, so that there was some enlargement of the areas of baldness, but this was not striking. It would appear, therefore, that perhaps only under circumstances in which growing hair is not mature or the mechanism of growth is unstabilized, as in alopecia areata, exhaustion of pigment-forming powers may cause loss of hair.

It is apparent that anthralin is effective in the treatment of alopecia areata, but it must be used with caution. From experience in these 2 cases it would seem that the chemical should be used in small concentration for perhaps one month to six weeks, alternated with agents of stimulating type but devoid of strongly reducing powers for similar periods.

SUMMARY AND CONCLUSIONS

Two patients with severe alopecia areata improved greatly under treatment with anthralin (dihydroxyanthranol-1, 8).

The too intensive and persistent use of this chemical productive of pigmentation eventually exhausted the pigment-forming properties of the skin, and coincidentally therewith all the regrown hair fell out.

Although this chemical is valuable in the treatment of alopecia areata, it may do more harm than good unless used with caution and for short periods.

In the light of reports in the literature of cases of alopecia areata and vitiligo appearing coincidentally, the phenomenon observed in the 2 cases reported has special interest from the standpoint of the relation between pigmentation and growth of hair.

401 Medical Arts Building.

TREATMENT OF PEMPHIGUS WITH CONCENTRATED VIOSTEROL

E. B. TAUBER, M.D.
AND
GEORGE E. CLARKE, M.D.
CINCINNATI

We do not propose to enter into the controversial subject of the cause of pemphigus. We wish merely to report on the more or less successful use of massive doses of viosterol in the treatment of this condition.

Ludy and his associates [1] reported 6 cases of successful treatment with viosterol in variable amounts, 12 to 45 cc. daily, during the height of the disease. These amounts correspond approximately to 120,000 and 450,000 international units of vitamin D daily. King and Hamilton [2] have recently reported the successful use of concentrated viosterol in a case of pemphigus vulgaris. The average daily dose used in this case during the clearing of the lesions was 400,000 units of vitamin D. The maintenance dose after the clearing of the lesions was 100,000 units.

Although the cause of pemphigus has not definitely been established, it may be reasonably supposed to be some form of toxic manifestation, either within the body or in the skin itself.

Bade [3] stated:

> A variety of toxic factors combine to produce pemphigus vulgaris. It is a question, however, whether the toxins come from a metabolic disturbance or are produced by (and reabsorbed from) the skin itself.

Recent experimental data indicate that large amounts of viosterol do no material or permanent harm.

From the Department of Dermatology and Syphilology, University of Cincinnati Medical School.

1. Ludy, J. B.; DeValin, C. M., and Hart-Drant, P.: Viosterol in the Treatment of Pemphigus, report from the Departments of Dermatology, Philadelphia General, Episcopal, Pennsylvania, Lankenau and Methodist Hospitals, Philadelphia.

2. King, H., and Hamilton, C. M.: Pemphigus Controlled by Vitamin D, Arch. Dermat. & Syph. **39**:515-517 (March) 1939.

3. Bade, W.: Lebertherapie beim Pemphigus vulgaris, Dermat. Wchnschr. **104**:389-392, 1937.

Shohl,[4] in commenting on the physiologic and pathologic effects of vitamin D, stated:

> When huge excesses of vitamin D are given, there results a definite pathologic condition called hypervitaminosis D. It is an exaggerated form of the physiologic or therapeutic effect of this vitamin. The calcium and the phosphate level in the blood are raised above normal. Calcification takes place at an increased rate, so that on roentgen or histologic examination the deposition of minerals at the provisional zone of calcification is unusually dense. When the dose is sufficiently large, about a thousand times the therapeutic dose, the deposition of minerals at the epiphyses is made at the expense of that in the shaft. The balances of calcium and phosphorus become negative. Metastatic calcification now takes place. The organs most affected are the tubules of the kidneys, blood vessels, heart, stomach and bronchi. There is evidence of irritation and degeneration in these tissues and in the liver. Under these conditions the animals lose weight rapidly, have intense diarrhea and die in from five to fourteen days.

Reed [5] reported in 1934 that the physiologic effects of massive doses of vitamin D are so different from those of small doses that the concentrated material should be considered tentatively as a different substance, at least until the mechanism of its action is fully understood. The results of a great deal of earlier work can at present be disregarded in a consideration of the effects produced by the highly purified preparations now available.

Dreyer and Reed,[6] in reporting the use of massive doses of viosterol in the treatment of arthritis, stated that in all cases of clinical benefit there were general improvement in nutrition, less evidence of vasomotor instability, greater muscular strength, less tendency to fatigue and improved gastrointestinal function. In all of their cases in which treatment with massive doses of viosterol was used over periods of two to five years there was no evidence of hypertension developing after continuous treatment.

Wyatt, Hicks and Thompson,[7] in reporting on the use of massive doses of viosterol for proliferative arthritis, stated that the morphologic blood picture did not alter more rapidly or distinctly; the calcium and the phosphorus level exhibited only minimal changes, and there was no significant change in the calcium-phosphorus ratio.

---

4. Shohl, A. T.: Physiology and Pathology of Vitamin D, J. A. M. A. **111**:614-619 (Aug. 13) 1938.

5. Reed, C. I.: Symptoms of Viosterol Overdosage in Human Subjects, J. A. M. A. **102**:1745-1748 (May 26) 1934.

6. Dreyer, I., and Reed, C. I.: The Treatment of Arthritis with Massive Doses of Vitamin D, Arch. Phys. Therapy **16**:537-540, 1935.

7. Wyatt, B. L.; Hicks, R. A., and Thompson, H. E.: Massive Doses of Vitamin D in the Treatment of Proliferative Arthritis, Ann. Int. Med. **10**:534-536, 1936.

Heymann [8] demonstrated that five days after 20 cc. of viosterol, or 200,000 units of vitamin D, was given to rabbits there was an increase in the inorganic phosphorus content of the blood without any effect on the calcium content.

Morgan, Kimmel and Hawkins [9] reported as follows:

> Nine series of experiments on rats were carried out in an attempt to discover whether moderately excessive doses of irradiated ergosterol and of fish liver oil concentrates produce toxic symptoms similar in kind and severity. Irradiated ergosterol and concentrates of tuna liver oil and of cod liver oil along with a basal diet of constant composition were administered at levels of 4000 and 10,000 international units of vitamin D daily for periods of 21 to 57 days, after which serum calcium and inorganic phosphorus, bone ash, lung, heart, and kidney calcium and phosphorus content were determined. In some cases representative animals were sacrificed at 14 day intervals in order to follow the course of the changes induced.
>
> In comparable animals lower percentages of femur ash and higher calcium and phosphorus contents of the soft tissues were usually found in those given the irradiated ergosterol than in those given the liver oil preparations. More deaths and greater interference with growth were observed also in the former group.
>
> The effects of sex and of varying vitamin A intake upon hypervitaminosis D were studied also. No difference due to sex, apart from that ascribable to size, could be detected, but definite alleviation of symptoms was observed when large amounts of vitamin A, 2500 to 23,000 international units daily, were administered. No toxic effects of the large doses of vitamin A were seen.

Farley,[10] in using viosterol in the treatment of arthritis, noticed that toxic signs of nausea and increased micturition followed the administration of from 600,000 to 1,000,000 units of vitamin D per day, but stated that toxic symptoms seldom developed if the dose remained under 400,000 units.

For the past four years the dermatologic staff at Cincinnati General Hospital and clinicians in other cities have been using massive doses of viosterol [11] in the treatment of pemphigus. The patients presenting themselves for treatment were given a dose of from 100,000 to 500,000 units of vitamin D each day. The smaller dose was given only to make sure that the patient could tolerate the drug and was maintained for only two to seven days and then increased.

---

8. Heymann, W.: Mode of Action and Metabolism of Vitamin D, J. Pediat. **8**:480-488, 1936.

9. Morgan, A. F.; Kimmel, L., and Hawkins, N. C.: A Comparison of the Hypervitaminoses Induced by Irradiated Ergosterol and Fish Liver Oil Concentrates, J. Biol. Chem. **119**:lxx-lxxi, 1937.

10. Farley, R. T.: Management of Arthritis, Illinois M. J. **71**:74-77, 1937.

11. The viosterol was furnished by the Wm. S. Merrell Co.; it was prepared by the Sperti process and put up in capsules each containing 50,000 units of vitamin D.

In all the cases to be reported the only toxic signs were nausea, a slight increase in micturition and diarrhea. These toxic symptoms apparently had no relation to the size of the dose and disappeared rapidly with discontinuance of the drug and administration of small amounts of yeast. After the disappearance of the toxic signs the patients were again given massive doses of vitamin D and were able to tolerate similarly large doses.

REPORT OF CASES

CASE 1.—W. C., a white man aged 60, entered the Hamilton County Home and Chronic Disease Hospital on Oct. 18, 1937, with a diagnosis of pemphigus, hypertension and arteriosclerosis. Examination at entrance disclosed no ulcerations in the mouth, but typical lesions of pemphigus on the face, hands, legs and chest. Soon after entrance concentrated viosterol therapy was started and by November 24 he was taking 500,000 units of vitamin D daily. This dose was maintained until December 6, when examination disclosed that all the lesions except a few on the neck and arms were healed. From then on a daily average dose of from 100,000 to 200,000 units was maintained until Feb. 15, 1938. At that time great improvement was evident, only an occasional crusted lesion on the neck remaining.

At this time the viosterol was discontinued for several weeks, and then medication was started again, with a dose of 50,000 units of vitamin D per day. Bronchial pneumonia later developed, and the patient died.

Necropsy showed no essential abnormality except for the gross signs of arteriosclerosis and hypertension.

CASE 2.—R. C., a white man aged 64, was admitted to the Cincinnati General Hospital on Sept. 19, 1936, with the statement that the eruption had started about five or six months before admission. The initial lesion occurred in the left lower quadrant of the abdomen, was raised and erythematous and itched. He was unable to give any date when the vesicles first appeared.

On his admission to the hospital, lesions were found on the abdomen, chest, head and extremities. These consisted of vesicles arising from a clear skin and crusts following rupture of the vesicles. The new vesicles contained clear serum, which in the course of a few days became cloudy.

During the first few days' hospitalization new vesicles about 2 cm. in diameter formed on the chest, arms and head. Nikolsky's sign was present. Laboratory tests gave negative results. During the patient's stay in the hospital viosterol yielding 100,000 units of vitamin D was given daily.

Before he was transferred to the Hamilton County Home and Chronic Disease Hospital, on Jan. 15, 1937, no new lesions had appeared for several weeks, and the old lesions had crusted and dried. During his stay no viosterol was administered. On February 4 he died of acute coronary thrombosis.

Necropsy showed lobular pneumonia, portal cirrhosis, acute splenitis, arteriosclerosis and atrophic arthritis. The spleen weighed 385 Gm. and was covered by a thin, slate-colored capsule. Sections through this organ revealed a soft, pultaceous, pinkish red, extremely friable parenchyma, in which the fibrous and follicular markings were obliterated. The liver weighed 1,730 Gm. Sections revealed an extremely firm, moderately irregular, mottled grayish pink cut surface transversed by thin pale gray bands. The surface of the liver was irregular under the capsules. Both kidneys were of normal weight and appeared normal macroscopically.

CASE 3.—J. H., a white woman aged 70, was admitted to the hospital from the dermatologic clinic on Nov. 10, 1934, with the history of having first noticed lesions on her legs about four months before. These consisted of vesicles which became turbid and broke, leaving a reddened area beneath.

On admittance she had lesions scattered over the entire body, with a few on the face. They consisted of reddened patches of various sizes with scaling around the margins. There were a few bullous lesions on the leg, arising out of apparently normal skin and not surrounded by an areola. These were filled with cloudy fluid. There were some suggestive lesions on the left cheek. Laboratory examination revealed no abnormalities of the blood or urine.

Treatment at first consisted of application of 1 per cent methylrosaniline (gentian violet) to all the lesions. From Nov. 20, 1934, to March 23, 1935, she was given 40,000 units of vitamin D three times daily, after which the amount was reduced to 20,000 units twice daily. This medication was discontinued on June 15, and a maintenance dose of 4 fluidrachms (14.79 cc.) of U. S. P. cod liver oil was given twice daily until she was transferred to the Hamilton County Home and Chronic Disease Hospital, on October 3. Nikolsky's sign had been present during her stay in Cincinnati General Hospital.

After admission to the latter hospital, she was again given concentrated viosterol sufficient to furnish 100,000 units of vitamin D per day until June 8, 1936. At this time all the lesions had cleared. The Pels-Macht test on Jan. 4, 1936, showed a reading of 57 per cent. She was discharged on June 8.

The patient was readmitted to the Hamilton County Home and Chronic Disease Hospital on Jan. 22, 1937, and was given variable amounts, from 50,000 to 300,000 units, of vitamin D daily until her death, on September 2, of bronchial pneumonia.

Necropsy showed cerebral softening, lobular pneumonia and fatty infiltration of the liver. The spleen was normal, weighing only 100 Gm. The liver, weighing 1,995 Gm., showed a smooth capsule. Section revealed the parenchyma arranged in the form of small yellow rings of uniform distribution, surrounded by small reddish areas. The pancreas was normal. Both kidneys were of normal size and showed no pathologic changes.

CASE 4.—E. B., a white woman aged 63, was admitted to the otorhinolaryngologic service in August 1934, with a diagnosis of stomatitis with ulcerative laryngitis. At that time she said she had noticed vesicles of the mouth which discharged bloody material and exfoliative epithelium when ruptured. The mouth was described as having numerous excoriated areas throughout, covered with a grayish membrane. Some of these lesions were similar to mucous patches. There was a definite erosion of the interarytenoid space, and the left cord of the larynx had jagged edges. She was discharged as improved but readmitted ten days later to the dermatologic service, with a discrete bullous eruption on the buttocks, legs and soles. Some lesions had recurred in the mouth. After admission on September 27 a few new lesions appeared; these were small and soon involuted.

The laboratory data were not remarkable. The calcium content of the blood was 8.3 mg. per hundred cubic centimeters. A roentgenogram of the chest disclosed some fibrosis along the vertebral trunks, and in the apexes no active lesions were found. Although the patient had latent syphilis, the Wassermann reaction of her blood and of her spinal fluid were negative. The phytopharmacologic test showed a reading of 50 per cent for the blood and of 65 per cent for the spinal fluid, indicating toxicity. Urinalysis and blood counts gave results within normal limits. Medication consisted of seven injections of 2 Gm. of tryparsamide. A solution of 1 per cent methylrosaniline was applied to the lesions on the legs.

On October 17 administration of cod liver oil three times daily in a dose representing 4,000 units of vitamin D was started. This was continued until Nov. 16, 1937, when treatment with ½ fluidrachm (1.8 cc.) of viosterol three times a day, representing a total of 60,000 units of vitamin D, was instituted. The dose was increased on Jan. 27, 1935, to 120,000 units of vitamin D daily, which was continued until her discharge.

She was discharged to the dermatologic clinic on March 13. At that time the lesions were almost completely healed. She was followed in the clinic until the end of January 1936, when she failed to return.

CASE 5.—M. J., a Negress aged 47, was admitted to the ward from the dermatologic clinic on Aug. 24, 1937. Lesions started as small blisters on the abdomen and thorax about three months before admission. On admission she had small and large bullae over the entire body. These were filled with cloudy fluid. Other areas, the sites of previous bullae, were darkened with a scaly margin. Nikolsky's sign was present.

The Kahn reaction was 3 plus. The phosphorus content of the serum was 4 mg. per hundred cubic centimeters and the calcium content 9.2 mg. Blood culture was negative. Culture of fluid from bullae showed Staphylococcus aureus. The phenolsulfonphthalein test showed normal hepatic function. The phytopharmacologic test gave a reading of 52 per cent. Both blood counts and urinalyses gave negative results. Local treatment consisted of applications of boric ointment to the entire body. Four transfusions with a total of 1,200 cc. of blood and 800 cc. of saline solution were given.

On August 26 administration of 50,000 units of vitamin D three times a day was begun. The dose was increased on September 11 to 100,000 units of vitamin D three times a day. The patient was discharged to the dermatologic clinic on November 24, on a regimen of 50,000 units of vitamin D per day.

This patient was followed in the dermatologic clinic and was last seen in December 1938. She had had a maintenance dose of 50,000 units per day on the average of four to five days each week since her discharge from the hospital. No new lesions had appeared since her discharge, but there was scaliness of the skin over the arms, legs and back. The patient stated that she had been well since her discharge from the hospital.

CASE 6 (reported by Dr. C. C. Barrett, Lexington, Ky.).—A white woman aged 63 had had pemphigus vulgaris for twelve years. She weighed approximately 130 pounds (59 Kg.). The pemphigus had been so severe that with the exception of a few weeks the patient had spent the last five or six years in bed. At the time she began to take viosterol, in January 1938, she had not been out of bed for fifteen months. She gradually increased the dose of viosterol to 10 capsules of vitamin D (500,000 units) a day. She took the preparation for almost six weeks before showing any improvement and then rather suddenly began to improve. At about the same time she suffered from frequency of urination and was so badly nauseated that she could retain no food but was able to be out of bed. Her skin returned to normal within a few weeks after it first started to clear. The dose was then reduced to 4 capsules (200,000 units of vitamin D) a day, and she had a relapse. Recently the dose was increased to 6 capsules (300,000 units of vitamin D) a day, with some improvement in her skin, although it is not entirely clear at the time of this report and she continues to have a few blebs. With this dose (6 capsules a day) the patient has not had frequency of urination or nausea.

CASE 7 (reported by Dr. Morris Lavin, Philadelphia).—A. M., a white married woman aged 58, was seen first in October 1935, complaining of sore throat and

weakness. Examination revealed a ragged ulcerative area over the tonsils and posterior laryngeal wall. The tonsils were enlarged and infected. She appeared extremely undernourished and underweight, and her weight was found to be 98 pounds (44.5 Kg.). She was given a high vitamin diet and vitamin therapy. No local treatment was given. Vincent's organisms were not found in repeated smears of material from the throat. After one week the condition of her throat cleared.

She was not seen again until November 25, at which time a bleb had formed near the umbilicus. At this time it was learned that she had stopped her previous treatment as soon as the sore throat disappeared. Examination at this time revealed the same type of lesion in the throat as previously. A diagnosis of pemphigus was made with the condition of the throat as part of the picture. The previously described treatment was resumed. The next day there was a generalized eruption of blebs over the entire body. Consultation verified the diagnosis of pemphigus. The consultant suggested larger doses (4 cc. of viosterol daily). After two days on this dose she manifested intolerance to the drug in that form by nausea and vomiting. Concentrated viosterol capsules were suggested. An average dose of 150,000 units of vitamin D per day was used. After three weeks of treatment her lesions disappeared completely. She had gained 11 pounds (5 Kg.).

In December 1936 she moved from this city and trace of her was again lost. It was recently learned from her son that she died several months ago of pneumonia and that there had been no return of the cutaneous lesions. During the interim she had been using the capsules but in a lesser number.

Case 8 (reported by Dr. Morton Morgenstern, Cleveland).—A man aged 54 was found to have some lesions in the throat. Thinking they represented Vincent's infection, the physician gave him neoarsphenamine intravenously. In the course of time bullae broke out over the entire body. The patient was taken to the hospital and given a blood transfusion and then viosterol equivalent to 200,000 units of vitamin D daily. He received the routine care for these lesions, which became secondarily infected. He was in the hospital for approximately three weeks and was then taken home. He continued to have 200,000 units of vitamin D in the form of viosterol daily. After about six weeks all the lesions cleared, and the patient, who had lost approximately 60 pounds (27 Kg.), regained most of it over three months.

He then had some teeth extracted. A week after this he did not feel well and again began to note lesions of the mouth. He was then sent to City Hospital, Cleveland, and succumbed to the disease about five weeks later.

The final diagnosis was pemphigus and secondary bronchial pneumonia.

Case 9 (reported by Dr. Frank W. Burge, Philadelphia).—J. J. M., a white man aged 52, was first seen on Aug. 11, 1936, with typical lesions of pemphigus on the skin and tremendous ulceration of the tongue with necrotic areas 1 or 2 cm. in diameter. He was given 350,000 units of vitamin D daily in the form of viosterol until March 11, 1937, at which time the lesions had cleared completely except for several slight relapses that quickly disappeared. When the patient was last heard from, on Nov. 30, 1937, he stated that he was still taking viosterol but had had one or two minor relapses. He also stated that his general health had improved greatly.

COMMENT

Nine cases of pemphigus (the diagnosis was confirmed in all by consultation) in which massive doses of concentrated viosterol had been administered are reported. In all but 1 case great alleviation of symp-

toms and either partial or total disappearance of the cutaneous lesions were noted.

Three of the patients died after having received viosterol from one to three years. The cause of death in all 3 cases apparently was not related directly to the eruption. Necropsy showed no apparent calcium deposits in any of the organs examined macroscopically. Examinations of blood during administration of massive doses of concentrated viosterol have not demonstrated any material change in the calcium and the phosphorus content or their ratio.

It is felt that on the basis of previous reports and on the basis of our own experience massive doses of vitamin D afford a simple and effective means of controlling the cutaneous lesions of pemphigus, even though these lesions reappear with all their former severity if a maintenance dose of vitamin D is not continued during periods of observation. Reactions during the administration of massive doses of vitamin D have been mild and have been well controlled by discontinuance of the medication and the concomitant administration of small doses of yeast. It was found that after the recovery from these reactions the patient could build up a tolerance to a large dose of vitamin D without further difficulty.

Clinical Notes

SYNTHETIC TAR PASTE

A Therapeutic Suggestion

W. H. Guy, M.D.; F. M. Jacob, M.D., and Frank Weber, Ph.G., Pittsburgh

The efficacy of crude coal tar as a topical application is attested by the favorable clinical experience of dermatologists throughout the world. Patients object to its uncleanliness and staining qualities. Furthermore, different lots of crude coal tar vary materially in composition. Feeling that a preparation free of these objectionable qualities and with equivalent therapeutic effect would be distinctly advantageous, we have elaborated a synthetic tar by ascertaining the average formula of crude coal tar and eliminating inert and irritating substances, a classification which, as will be noted, includes 44.7 per cent pitch.

The following constituents have been identified in coke oven coal tar produced in the United States:

Light Oil	Per Cent
Crude benzene and toluene	0.3
Coumarone, indene, etc.	0.6
Xylene, cumenes and isomers	1.1
Middle and Heavy Oils	Per Cent
Naphthalene	10.9
Unidentified oils in the range of naphthalene and methylnaphthalenes	1.7
α-Monomethylnaphthalene	1.0
β-Monomethylnaphthalene	1.5
Dimethylnaphthalenes	3.4
Acenaphthene	1.4
Unidentified oils in range of acenaphthene	1.0
Fluorene	1.6
Unidentified oils in range of fluorene	1.2
Anthracene Oils	
Phenanthrene	4.0
Anthracene	1.1
Carbazole and kindred nonbasic nitrogen-containing bodies	2.3
Unidentified oils in range of anthracene	5.4
Phenol	0.7
Phenol homologues (largely cresols and xylenols)	1.5
Tar bases (mostly pyridine, picolines, lutidines, quinolines and acridine)	2.3
Yellow solids of pitch oils	0.6
Pitch greases	6.4
Resinous bodies	5.3
Pitch (460 F. fusing point)	44.7
Total	100.0

From the Department of Dermatology of the University of Pittsburgh School of Medicine.

Using these figures as a guide, we have prepared a synthetic tar containing quantities of active ingredients equivalent to those contained in the original coal tar, the ratio being corrected in keeping with elimination of the inert substances and the irritating light oils.

Synthetic Tar (Basic Formula)	Per Cent
Anthracene [1]	1.10
Naphthalene	10.90
Phenanthrene	4.00
Carbazole	2.30
Picolene, Pyridine, Quinolene, each	0.58
Phenol	0.70
Cresol	0.75
Petrolatum, To make	100.00

The formula just given may be used in various preparations in the same percentages as crude coal tar. The following formula is one we frequently use:

	Gm.
Synthetic tar	2.0
Solution of aluminum acetate	5.0
Wool fat	10.0
Paste of zinc oxide with salicylic acid (N. F.)	30.0

7026 Jenkins Arcade.

1. The anthracene used was obtained from the Fisher Scientific Company, 709-719 Forbes St., Pittsburgh, labeled "Anthracene (40%) (Technical)."

DERMATITIS DUE TO STYLE OF HAIRDRESS

HAROLD SHELLOW, M.D., CHICAGO

A woman 24 years old presented a dermatitis on the back of the neck which had been present for about five months. She had applied nothing but zinc oxide ointment occasionally. It was her habit to go to a beauty parlor each week to receive a hair wash and set, but she stated that she had not used any form of dye or coloring compound. She said that the eruption itched only mildly.

Examination disclosed an eruption on the back of the neck, consisting of a diffuse, roughly outlined patch of dull red dermatitis. It was moderately lichenified and slightly scaly. The lesion was oval and measured 4 by 1½ inches (10 by 4 cm.). Inspection of the scalp showed no evidence of seborrheic scaling, and the common sites for seborrheic eczema on the face were free from any eruption. The patient wore a "page boy" type of hairdress, the hair hanging down in an unbroken mass. The ends of the hair were curled under in one continuous roll, shaping to the neck and touching the skin at the lowest point in the back. It was noticed that any normal movement of the head caused the roll of hair to

sway from side to side, thereby producing contact with the skin at right angles to the hair. In the presence of the setting fluid, which somewhat stiffened the hair, one could observe a grasping or razor-like action the curl was causing against the skin.

A patch test with the hair-setting fluid made on the side of the neck gave negative results. It was suggested that she change her coiffure so that no contact would be made between the skin and the hair on the back of the neck. She was advised to continue going to the beauty parlor. A bland ointment was prescribed for use at night.

After a week of this form of management the dermatitis showed definite improvement and when she was seen two weeks later no evidence of the eruption except faint pigmentation was visible. A month later, when she was again seen, a small linear patch of dermatitis had developed in the location previously affected, but of about one-fourth the dimensions of the former spot. She admitted that for the past two weeks she had again worn her hair in "page boy" fashion. Prompt relief was brought about by changing the hair style again.

COMMENT

This case is reported to disclose that dermatitis may result from the irritating action of one's hair against the skin. In this case it was brought about by friction caused by a "page boy" hairdress to which a setting fluid had been applied to preserve its shape.

185 North Wabash Avenue.

CONTACT DERMATITIS DUE TO PONTOCAINE HYDROCHLORIDE

LESTER HOLLANDER, M.D., PITTSBURGH

Dr. W. M., an otorhinolaryngologist aged 58, consulted me on account of "cracked fingers" of several years' duration. The lesions consisted of deep longitudinal fissures, which started at the tip of each involved finger and extended to the base of the distal phalanx; the skin about the fissures was red, somewhat soggy and crusted.

The left thumb and index and middle fingers, the tip of the right thumb and the right index finger were involved, and there was also a fissured longitudinal area of about 2 cm. on the left hypothenar eminence. The areas on the left hand were much greater in extent and in intensity.

Washing and especially scrubbing of the hands caused a great deal of pain and inconvenience and played havoc with the patient's surgical schedule.

He volunteered the information that after a day of rest from his work, as on a Monday morning, his fingers were definitely on the mend.

The sharp delineation of this disease, his occupation and the history of improvement on Monday morning strongly suggested the possibility of a contact dermatitis.

The areas involved corresponded with the sites where medicated cotton applicators came most frequently in contact with his hands. He used a metal probe as a cotton carrier, and he wound and unwound pledgets of cotton on it for the

---

Submitted for publication, April 22, 1939.
From the Pittsburgh Skin and Cancer Foundation.

purpose of inserting medicaments in the nose, the supply cotton being held in the hollow of his left hand.

Cutaneous tests were made with cotton and the medicaments which he used on the applicator, including iodized oil, synephrin tartrate (parahydroxyphenylmethylaminoethanol tartrate), pontocaine hydrochloride, efemist and iso-efemist (proprietary preparations containing small amounts of ephedrine and chlorobutanol) and soap chips.

In twenty-four hours a decided reaction was found at the site of the test with pontocaine hydrochloride.

A careful history, the limitation of the eruption and patch tests established the cause of a long-standing and annoying disease of the skin.

News and Comment

THE AMERICAN BOARD OF DERMATOLOGY AND SYPHILOLOGY

The written examination of the American Board of Dermatology and Syphilology will be held in various large cities in the United States on Monday, Oct. 9, 1939. The oral examination will be held in Philadelphia on Friday and Saturday, November 3 and 4.

Applications must be received by the secretary, Dr. C. Guy Lane, 416 Marlboro Street, Boston, not later than Sept. 1, 1939.

Abstracts from Current Literature

EDITED BY DR. HERBERT RATTNER

COMPARATIVE STUDY OF TUBERCULIN PATCH TEST AND MANTOUX INTRACUTANEOUS TEST. HERMANN VOLLMER and ESTHER W. GOLDBERGER, Am. J. Dis. Child. **56**:584 (Sept.) 1938.

The authors have already demonstrated that their tuberculin patch test is at least equal, if not superior, to Pirquet's. In this article they state that they found that of 169 children with active tuberculosis only 1 failed to react positively to the tuberculin patch test who reacted positively to the Mantoux test with the stronger solution of purified protein derivative.

They further found that among 118 children admitted to the wards with various diseases, the Mantoux test, even when 1 mg. of old tuberculin was used, did not reveal a single case of tuberculous infection which had not already been discovered by the tuberculin patch test.

None of the patch tests, although some were performed on patients with extremely active tuberculosis, produced any general constitutional reaction.

HUMAN PASSIVE TRANSFER ANTIBODY: STUDIES ON CHILDREN HYPERSENSITIVE TO FOODS. VERNON W. LIPPARD and WILLIAM M. SCHMIDT, Am. J. Dis. Child. **56**:797 (Oct.) 1938.

The purpose of the authors' investigation was to study the response of the passive transfer antibody titer to ingestion of foods by hypersensitive children and to evaluate the hypothesis that an increase in titer is associated with relief from clinical symptoms after subsequent exposure.

In a number of instances ingestion of a specific antigen was followed by clinical symptoms such as urticaria and angioneurotic edema. Within three weeks there occurred a decided rise in antibody titer, and as long as the titer remained high the patient could consume food without ill effects—that is, food which originally caused clinical manifestations. These observations suggested, first, that the passive transfer antibody may increase in response to stimulation and, second, that freedom from clinical symptoms following subsequent contact with antigen may be associated with an increase in titer. Such work tends to show that this refractoriness to anaphylaxis was obtained by antianaphylaxis—a state in which there are sufficient free antibodies in the circulating blood to unite with all the antigen, so that it cannot reach the sensitized tissues.

MULTIPLE CYSTIC TUBERCULOSIS OF BONES IN CHILDREN. JOHN L. LAW and W. S. PERHAM, Am. J. Dis. Child. **56**:831 (Oct.) 1938.

The interest of this paper to the dermatologist lies in the fact that the disease described is the same as Jüngling's osteitis tuberculosa multiplex cystica. This affects chiefly the metacarpal and metatarsal bones and the phalanges, where it produces circumscribed "honeycombed" areas of rarefaction without any sclerosing reaction, periostitis or sequestration.

Dermatologists have been prone to associate this disease with Boeck's sarcoid, but Law and Perham point out that the associated cutaneous lesions in order of their likelihood are lupus pernio, Boeck's sarcoid, lupus vulgaris, lupus exfoliativus, Bazin's erythema induratum and scrofuloderma. However, such cutaneous lesions are usually not present in children, and they may appear only after the disease has been present for several years.

TREATMENT OF PERITONEAL SYNDROME AND ERYSIPELAS-LIKE LESIONS OF SKIN IN NEPHROSIS. C. A. ALDRICH and H. H. BOYLE, Am. J. Dis. Child. **56**:1059 (Nov.) 1938.

The chief interest of this article to the dermatologist is the fact that erysipelas-like lesions of the skin occur as a complication of nephrosis. This complication was described by Keefer and Yang in 1930 as follows:

"A patient with the typical signs of nephrosis suddenly develops fever, chilliness, and in some instances abdominal pain, nausea and vomiting. . . . Soon after the onset of fever, the patient usually complains of pain in the back, and it is particularly noticeable in the lumbar region. When the painful area is examined, no objective changes may be observed. Within twelve to twenty-four hours after the onset there is exquisite tenderness over the painful area with signs of acute inflammation of the edematous skin and subcutaneous tissues. The skin is red and the local temperature increased. The erythematous area varies in size, and in the beginning it may not be more than two or three centimeters in diameter. The edges are not raised and the tenderness extends over a greater area than the redness. This inflammation spreads peripherally with amazing rapidity and it is difficult for the patient to find a comfortable position in bed on account of the pain and tenderness. It is characteristic for the inflammation to spread and migrate into the most dependent parts."

Such erysipelas-like lesions occur on the lower part of the trunk, the lower extremities and the genitalia but never higher. In some series of cases of nephrosis, this erysipelas-like cutaneous lesion has existed alone; in other series it usually has been accompanied with symptoms of peritonitis. All the patients who had erysipelas-like cutaneous lesions recovered after large doses of convalescent serum for erysipelas or scarlet fever.

SULFANILAMIDE ERUPTION: STUDY OF PATIENTS WITH MORBILLIFORM RASH AND OF THEIR SUBSEQUENT REACTIONS. EDWARD R. SCHLESINGER and WALTER L. MITCHELL JR., Am. J. Dis. Child. **56**:1256 (Dec.) 1938.

Ten cases of dermatitis medicamentosa due to sulfanilamide were carefully studied to determine the nature of the eruption, the blood picture with special reference to the leukocytes, the clinical course of the exanthem and manifestations after readministration of the drug.

The authors propose a "natural history" of the eruption which emphasizes (1) a prodromal fever, sometimes preceded by transient leukopenia; (2) a morbilliform eruption most commonly appearing on the ninth day (from the fifth to the seventeenth day) of sulfanilamide therapy and lasting from thirty-six to ninety-six hours, and (3) splenomegaly in many cases.

Later administration of the drug produced a scarlatiniform eruption with fever and leukocytosis within a few hours. Continued administration was associated with evidence of increased capillary fragility and occasionally with arthritic phenomena. Unlike the reactivity to most drugs, that to sulfanilamide was decreased or abolished by passage of time, gradual increment of the dose over a short period or repeated administration of large doses at intervals.

The authors compare the apparent syndrome produced by sulfanilamide with "nirvanol (sodium phenylethylhydantoin) sickness."

TWO CASES OF PELLAGRA TREATED WITH NICOTINIC ACID. RICHARD FRANCE, ROBLEY D. BATES JR., W. HALSEY BARKER and EDWARD MATTHEWS, Bull. Johns Hopkins Hosp. **63**:46 (July) 1938.

Two cases of pellagra are reported in which the administration of nicotinic acid caused a prompt disappearance of lesions on the skin and mucous membrane.

The general strength and mental status were also much improved. The low cost of nicotinic acid, as compared with that of liver extract, yeast and wheat germ, means a tremendous reduction in the expense of treating pellagra. In 2 cases postoperative glossitis responded promptly to treatment with nicotinic acid.

NELSON PAUL ANDERSON, Los Angeles.

PEPTIC ULCER IN SYPHILIS OF CENTRAL NERVOUS SYSTEM. E. H. PARSONS, D. E. PLUMMER, J. R. EWALT and R. C. GASKILL, J. A. M. A. **110**:1991 (June 11) 1938.

In a statistical study, Parsons, Plummer, Ewalt and Gaskill noted that 21 of 200 patients who had syphilis of the central nervous system also suffered from peptic ulcer. This incidence (10.5 per cent) was compared with that of peptic ulcer in patients with latent syphilis, in patients with pulmonary tuberculosis and in a series of consecutive patients admitted to the hospital. In the three latter control groups the percentage incidence was 1.5, 1 and 3, respectively. The high incidence of peptic ulcer in patients with syphilis of the central nervous system was considered not directly due to the syphilitic infection, but the possibility was advanced by the authors that abnormalities due to involvement of the central nervous system and of the vascular system might be responsible.

CUTANEOUS ABSORPTION OF SEX HORMONES. C. R. MOORE, J. K. LAMAR and N. BECK, J. A. M. A. **111**:11 (July 2) 1938.

Moore, Lamar and Beck employed testosterone and testosterone propionate in a concentration of 50 mg. per ounce of cream in experimental studies with animals. They found that when applied to the skin both substances are readily absorbed and may exert the same effects as though injected subcutaneously. Thus in laboratory animals it was possible by applying the hormone through the intact skin to (1) maintain the accessory reproductive organs of castrate males, (2) reconstitute castrated guinea pigs within seven days of treatment to a state of producing coagulable ejaculates on electrical stimulation of the head and (3) injure the testes of normal growing young male rats. A commercial face cream containing estradiol and recommended for the removal of wrinkles, when rubbed into the skin of experimental animals, produced (1) mammary development in normal male guinea pigs, (2) reduction of the weight of the testes by 80 per cent and of the weight of the seminal vesicles by 90 per cent in young male rats, (3) cornified vaginal estrous smears in spayed female rats and (4) maintenance or increase in the normal growth of the uterus in young or mature spayed rats.

JAUNDICE FROM BISMUTH COMPOUNDS USED IN THERAPY OF SYPHILIS. R. NOMLAND, E. A. SKOLNIK and L. L. MCLELLAN, J. A. M. A. **111**:19 (July 2) 1938.

According to Nomland, Skolnik and McLellan, the possibility that jaundice is due to a bismuth preparation when it occurs during the treatment of a patient with syphilis has not previously received much consideration. Of 75 cases of jaundice occurring during treatment observed by the authors, in 32 the disease was thought to be due to a bismuth compound. In 10 no other drug had been given; in the remainder neoarsphenamine had been used, but in none within twelve weeks of the onset of the jaundice. In all cases the jaundice began within six weeks after the last treatment. There was no fatality in the series, and most patients were subsequently given a bismuth compound without any evidence of intolerance.

DERMATITIS CAUSED BY DIETHYLENE GLYCOL IN TOBACCO. B. A. NEWMAN, J. A. M. A. **111**:25 (July 2) 1938.

Newman reports the case of a white man aged 39 on whose left index and middle fingers and the left side of the upper lip an eczematous rash developed. A patch test with one of the three brands of cigaret tobacco used by the patient revealed cutaneous sensitivity. This tobacco contained diethylene glycol. When subsequently tested with this compound, the patient showed a reaction, whereas 2 control subjects did not. Cure occurred within two weeks after he stopped using this brand of cigaret tobacco.

SIGNIFICANCE OF POSITIVE KLINE EXCLUSION TEST UNCONFIRMED BY KOLMER OR KAHN TEST. R. M. MYERS and C. A. PERRY, J. A. M. A. **111**:142 (July 9) 1938.

Myers and Perry discuss the results of serologic tests with a sensitive antigen emulsion (Kline exclusion) when compared with the results of the Kolmer and the Kahn test. Of 234 specimens which gave a positive result with the Kline exclusion antigen and negative results with the Kolmer and the Kahn antigen, 26, or 11.1 per cent, were from patients with syphilis and 16, or 6.8 per cent, from patients who had been exposed to the disease. In the remainder the diagnosis was doubtful; no harm is occasioned by the positive finding if it is realized that confirmation by other serologic tests must be undertaken.

HEREDITARY MULTIPLE TELANGIECTASIS WITH EPISTAXIS. G. H. O'KANE, J. A. M. A. **111**:242 (July 16) 1938.

O'Kane reports the case of a man aged 71 who had had frequent nosebleeds since childhood. His father also suffered from frequent and severe epistaxis. The patient's hemorrhages became more severe as he approached middle life. Previous treatment to control the bleeding had included application of radium, nine intranasal operations and packing. It had been necessary to give him a transfusion of blood on one occasion. O'Kane reports the gradual eradication of the varices with subsequent freedom from hemorrhage from the repeated injection of a 5 per cent solution of quinine and urethane (ethyl carbamate). The solution was injected to raise a small bleb along the vessel. The nose was then firmly packed with bismuth glycerin gauze, which was removed in twenty-four hours. Varicosities were present on the face, in the nose and under the tongue.

TREATMENT OF SYPHILITIC PRIMARY OPTIC ATROPHY. J. E. MOORE, A. C. WOODS, H. H. HOPKINS and L. L. SLOAN, J. A. M. A. **111**:385 (July 30) 1938.

Moore, Woods, Hopkins and Sloan report the results of a statistical study of the results of treatment of 191 patients who had primary atrophy of the optic nerve due to syphilis. The patients were carefully selected and studied by members of both the syphilologic division and the department of ophthalmology of the Johns Hopkins Hospital. When the patient was untreated or received inadequate routine therapy, complete blindness occurred within seven years. Adequate routine antisyphilitic therapy caused delay in the development of blindness or occasionally arrest of the atrophic process. The results were good in 50 per cent of cases when subdural treatment by the Swift-Ellis technic was employed; in 10 per cent sudden blindness was caused by the treatment. The best results were obtained when malaria therapy was used; in about 85 per cent of cases the process was arrested. If only one eye was involved, the prompt initiation of treatment prevented involvement of the second eye in 70 per cent of cases.

TREATMENT OF CHANCROID WITH SULFANILAMIDE. B. A. KORNBLITH, A. JACOBY and M. WISHENGRAD, J. A. M. A. **111**:523 (Aug. 6) 1938.

Of 45 cases of proved chancroid, cure was obtained without exception, by the end of two weeks' treatment with sulfanilamide. The dose of the drug was 80 grains (5.2 Gm.) daily in divided doses for the first five days and 40 grains (2.6 Gm.) daily in divided doses for nine additional days. No complications or ill effects due to the treatment were noted. In cases observed for six months after cure there were no recurrences.

LEWIS, New York.

NEURODERMATITIS. G. MARCHMONT-ROBINSON, Urol. & Cutan. Rev. **42**:912 (Dec.) 1938.

The similarity of several of the symptoms of pernicious anemia to those of neurodermatitis drew the author's attention to the liver for the cause and treatment of the latter disease. Intramuscular injections of parenteral liver extract with vitamin B_1 produced rapid relief from the itching. After several such injections 3 patients suffering from neurodermatitis were completely well. Treatment was continued with a hematinic preparation with liver, given orally.

CARO, Chicago.

ETIOLOGY OF SEBORRHOEIC DERMATITIS. G. B. DOWLING, Brit. J. Dermat. **51**:1 (Jan.) 1939.

Dowling considers as essential two factors in the etiology of seborrheic eczema: the soil and the exciting cause. Included in the constitutional factors are functional instability of the skin with reference to its secretory functions, hypersensitivity to internal and external irritants, vasomotor instability and diminished resistance to infection. The same instability is found in mucous membranes. Endocrine imbalance and constitutional disposition to eczema are also factors. As to the exciting cause, he believes the available evidence points to a primary infection with yeastlike organisms, which are usually saprophytic but are capable of becoming pathogenic, and he points out that seborrheic eczema is particularly prone to undergo alteration due to secondary invasion by coccal organisms or other local constitutional factors.

AETIOLOGY OF SEBORRHEIC DERMATITIS. G. H. PERCIVAL, Brit. J. Dermat. **51**: 7 (Jan.) 1939.

Percival suggests that the term seborrheic eczema be dropped in favor of the following titles, to differentiate the eruptions at present covered by the term seborrheic dermatitis: (1) pityriasis capitis and eczematid lesions affecting the hairy or potentially hairy regions; (2) flexural dermatitis which is always exudative; (3) pustular dermatitis affecting areas covered with strong hair. All three groups represent distinct types of eczematous reaction different from the eczema produced by irritants from chemicals. Each group also has distinctive clinical features, bacteriologic findings and response to treatment. Flexural dermatitis usually has as its primary site the retroauricular region. In this type the staphylococcus and the streptococcus are constantly present, but it has not been possible to reproduce this type of flexural dermatitis by inoculating organisms derived from such lesions. The pustular type is also due to the staphylococcus, but in each group there is a distinctive reaction to the organism and frequently an idiosyncrasy.

PELLAGRA IN GREAT BRITAIN SINCE 1934. J. H. TWISTON DAVIES and H. GORDON MCGREGOR, Brit. J. Dermat. **51**:51 (Feb.) 1939.

The authors summarize cases of pellagra reported in Great Britain since 1934 and comment on the current theories of the cause of the disease. It is now generally

believed that the real factor is probably one of the constituents of the complex vitamin B_2, that it is water soluble and that it is present in liver extract from which both lactoflavin and vitamin B_6 have been removed by a special filtering process.

The authors point out, however, that vitamin B_2 deficiency alone is not sufficient explanation for the occurrence of pellagra in some cases. There have been cases reported in which the diet was reasonably full and varied, a point emphasized by exponents of the theory that the disease is infectious. The preponderance of the disease in the female sex points perhaps to the influence of endocrine secretions. Other factors, such as season and action of light, have some influence and finally, there is the possibility of association between pellagra and Addison's disease.

It would seem that vitamin deficiency might cause both pellagra and adrenal insufficiency in the same patient; that adrenal insufficiency might occur in the course of pellagra as a sequel to malnutrition, or that pellagra might occur in the course of chronic Addison's disease as a sequel to the associated anorexia.

NOTE ON PHYTOPHARMACOLOGICAL INDEX IN PEMPHIGUS. F. W. SANSOME and L. FORMAN, Brit. J. Dermat. **51**:63 (Feb.) 1939.

The authors performed the Pels-Macht phytopharmacologic test and found no statistically significant differences in the increments of growth of lupin seedlings in normal serum and in serum from patients with pemphigus. They suggest that an increased number of tests and a refinement of the technic are necessary before the Pels-Macht test can be used for practical purposes. The literature on the phytopharmacologic index in pemphigus is reviewed.

FURTHER EXPERIMENTAL STUDIES OF PEMPHIGUS. L. FLECK and F. GOLDSCHLAG, Brit. J. Dermat. **51**:70 (Feb.) 1939.

The authors attempted to confirm the work of Urbach, Brandt and Wolfram, whose experiments suggest a viral genesis of pemphigus. They concluded as follows:

"The suboccipital inoculation is an operation which by itself may lead to paralyses and lesions in the central nervous system without the action of infectious agents. These palsies can therefore not be used to prove a successful transmission of an infectious disease. Similarly the complement-fixation reaction of Urbach, Brandt and Wolfram should be regarded purely as an unspecific lability reaction. As the sole support of Urbach's theory remains the cross-immunity between pemphigus and rabies, as described by Schweinburg and Wolfram. Finally, we would like to make it quite clear that we are far from condemning the very attractive theory put forward by the Viennese workers. Our criticisms are mainly due to the experimental methods and their interpretation."

Suboccipital inoculations were then performed by Dr. Wolfram, and in a footnote the authors explain that Dr. Wolfram's interpretation of the results differs considerably from theirs, as he will probably report in a separate paper.

CASE OF CUTANEOUS AND CONJUNCTIVAL DIPHTHERIA. R. M. BATES, Brit. J. Dermat. **51**:76 (Feb.) 1939.

Bates reports a case in which the clinical picture at first suggested varicella. The formation of membranes on the conjunctivas finally led to a diagnosis of diphtheria. A cure was obtained after the administration of antitoxin.

A FAMILIAL CASE OF ACNE VULGARIS WITH LESIONS SUGGESTING A RELATIONSHIP OF ACNE CONGLOBATA. F. F. HELLIER, Brit. J. Dermat. **51**:109 (March) 1939.

Hellier presents evidence in the case of a 64 year old man that in cases of acne and related conditions the terrain is of an importance at least equal to that

of the types of infecting organisms in determining the character of the eruption. In his patient acne vulgaris appeared at puberty and has since spread so as to cover almost the whole body. In addition to the pustules of acne there were scars on the trunk and limbs, with "bridging" in some places, large infiltrated plaques on the buttocks oozing pus from fistulas, sebaceous cysts, rhinophyma and coarseness of skin. A study of this man's family revealed a group of symptoms which included lowered resistence to the organisms associated with acne, a tendency to comedo formation, excessive scarring, rhinophyma, sebaceous cysts, coarseness of skin and possibly mental slowness. One or more symptoms have been present in three generations, and the study suggests that these symptoms are dependent on some factors which are inherited as mendelian dominants.

TESTOSTERONE PROPIONATE IN ACNE VULGARIS. I. D. RILEY, Brit. J. Dermat. **51**:119 (March) 1939.

Testosterone propionate was used in the treatment of a small group of 20 patients for acne vulgaris; 8 were males and 12 were females. The general impression of the results in these patients in comparison with the controls was favorable, but no dramatic remissions were seen such as follow treatment with roentgen rays. There was no difference in response in the severe eruptions or in those previously treated with roentgen rays. The testosterone propionate was given in gradually increasing weekly doses up to 50 mg. per week, the average patient receiving about 300 mg. in three months' time. Riley concludes: "The burden of expense and an elaborate treatment of this type are only justified if the results are markedly superior to those obtained with simpler routine measures. This small series of cases does not suggest that any such remarkable results do follow the administration of testosterone propionate in acne vulgaris."

RATTNER, Chicago.

OSLER'S TELANGIECTASIA HAEMORRHAGICA HEREDITARIA. ALBIN PROPPE, Dermat. Wchnschr. **106**:233 (Feb. 26) 1938.

Proppe was able to trace through three generations the family tree of a couple both of whom had Osler's disease. In the second generation 4 of 9 members gave evidence of this disorder, and in the third, 3 of 13. Three suicides occurred.

INHERITANCE OF ECZEMA, ESPECIALLY NEURODERMATITIS. H. HRUSZEK, Dermat. Wchnschr. **106**:239 (Feb. 26) 1938.

Hruszek reports a case of neurodermatitis in which the patient's mother and 2 children had the same conditions. A second patient with neurodermatitis had 2 children similarly affected. The author believes that this disorder is apt to be inherited.

TREATMENT OF ULCUS CRURIS. SEPP TAPPEINER, Dermat. Wchnschr. **106**:353 (March 26) 1938.

Tappeiner describes his technic for the treatment of varicose ulcers by means of Thiersch grafts. He has been successful with the use of silver foil over the grafted area. Two typical histories are presented with "before and after" photographs.

UNUSUAL CASE OF ACRODERMATITIS CONTINUA (HALLOPEAU). GEORGE MAHN, Dermat. Wchnschr. **106**:363 (March 26) 1938.

Mahn describes a 48 year old man who had a recurring vesicular eruption on the hands and feet of seventeen years' duration. It was little influenced by treatment.

TAUSSIG, San Francisco.

CASE OF MULTIPLE CHANCRES. F. FRENZL Ceská dermat. **18**:39 (Feb.) 1938.

The patient presented a chancre at the root of the tongue and one at the posterior commissure, with submaxillary and right inguinal adenitis. Both primary lesions showed spirochetes on dark field examination. The Wassermann reaction of the blood was positive. The patient had had coitus per vaginam and per os on the same day.

SALT-FREE DIET IN TREATMENT OF TUBERCULOUS LUPUS. K. GAWALOWSKI, Ceská dermat. **18**:59 (March) 1938.

Observations made at Masaryk's institute for the treatment of lupus, Prague, Czechoslovakia, place salt-free diet among the most efficient adjunct therapeutic measures for this condition. Used alone, the dietary treatment is considered too expensive and time consuming. When combined with irradiation from the carbon arc lamp, the salt-free diet increases the response to the irradiation. The main advantage of salt-free diet lies in its favorable effect on the weight and the general condition of the patient.

PULMONARY TUBERCULOSIS AND ITS INFLUENCE ON HEALING OF TUBERCULOUS LUPUS. OLGA VALENTOVA, Ceská dermat. **18**:80 (March) 1938.

Of 110 patients with lupus vulgaris treated at Masaryk's institute, Prague, Czechoslovakia, 41 had more or less advanced pulmonary tuberculosis. Thirteen patients had lupus vulgaris in association with scrofuloderma and incipient pulmonary tuberculosis. In the others roentgen examination showed either calcified areas in the lungs or no evidence of tuberculosis. The activity of pulmonary disease did not prevent the healing of lupus vulgaris, as even in cases of open tuberculosis the cutaneous lesions often responded well to treatment. However, the number of cases of resistant lupus increased with the severity of pulmonary involvement. The healing of cutaneous lesions did not aggravate or reactivate the pulmonary process, as has been sometimes suspected.

SPINKA, Texarkana, Texas.

Society Transactions

NEW ENGLAND DERMATOLOGICAL SOCIETY

FREDERICK S. BURNS, M.D., *President*

Boston, Oct. 19, 1938

BERNARD APPEL, M.D., *Secretary*

A Case for Diagnosis and Suggestions as to Treatment (Pemphigus?). Presented by DR. C. GUY LANE, Boston.

This woman, aged 48, states that two months before entry to the hospital blotches developed on the inner aspect of the thighs and spread to the abdomen and back. The appearance of the lesions was preceded by a few days of malaise. Daily chills and sweating accompanied the eruption. One week before entry her mouth became so sore that eating was uncomfortable. Four days before entry a new crop of lesions appeared. There are generalized erythematous urticarial lesions varying from small blisters to lesions 2 cm. in diameter and larger. The larger plaques show central depression with rounded borders. Where the bullae have ruptured there are now weeping red spots, which heal to form flat pigmented spots.

Laboratory tests showed 12,900 white blood cells, with a differential count of 66 per cent polymorphonuclear leukocytes, 27 per cent lymphocytes, and 7 per cent mononuclears. The stool gave a positive reaction to the guaiac test. The urine showed the slightest possible trace of albumin. The blood calcium content was 9.04 mg. per hundred cubic centimeters.

Daily doses of 5 to 10 cc. of dihydrotachysterol ("A. T. 10") by mouth were given, and improvement was noted.

DISCUSSION

DR. J. L. GRUND, Boston: The patient presents a number of typical lesions of erythema iris in addition to bullae and additional erythematous lesions, all pointing to erythema multiforme bullosum rather than to pemphigus.

Sporotrichosis. Presented by DR. C. GUY LANE, Boston.

This woman, aged 65, states that one and one-half years ago a small persistent sore developed on the right fifth finger and has steadily progressed. One year ago a lesion appeared along the inner side of the right arm, with lumps in the axilla. These slowly subsided. She formerly presented extensive areas of erythema with heavy circular areas of verrucous crusting and fungation involving the dorsa of the hands, the fingers and the distal half of the dorsum of the forearm. Many areas were discharging pus. On the inner aspect of the right arm are numerous infiltrated dark red nodular granulomatous lesions in a roughly linear satellite-like distribution. The right axillary lymph nodes are enlarged, discrete, smooth and slightly painful.

Cultures from lesions showed Sporotrichum.

She did not respond to administration of 15 to 18 Gm. of potassium iodide daily, but responded slowly but definitely to treatment with ethyl iodide.

DISCUSSION

DR. C. GUY LANE, Boston: In the beginning there was a striking resemblance to blastomycosis, and I felt that the patient had blastomycosis and was much interested when the organism of sporotrichosis was found, I think, on three different occasions. This was demonstrated in the excellent smear which Dr. Ray prepared for presentation today.

DR. WILLIAM P. BOARDMAN, Boston: For my own information, I should like to know if anybody can tell me why this woman did not respond to potassium iodide. In the cases I have observed, the beneficial results have been striking.

DR. L. F.. RAY, Boston (by invitation): Of about 80 cases I have reviewed so far, I think there was a response in about 30 per cent. In about 30 or 40 per cent the condition recurred the moment the medication was stopped, but in none did it seem to be as resistant as in this case.

DR. JOHN GOODWIN DOWNING, Boston: The eruption on the dorsum of the hand in this case is unusual. The spores of this fungus are different from those of the organism in the case I reported (Surgical Problems of Fungous Origin: Report of a Case of Sporotrichosis in Massachusetts, *New England J. Med.* **212:** 1085 [June 6] 1935). Instead of the ovate or pearlike spore, this organism shows cigar-like spores arranged in the shape of a star. The case is most interesting and well presented.

DR. J. H. SWARTZ, Boston: The arrangement of spores here is characteristic of sporotrichosis. I shall admit that the shape is described in the textbooks as that of a pear, but one rarely sees that shape. This shape is more likely. The members have witnessed an excellent demonstration of a smear of sporotrichosis.

DR. FREDERICK S. BURNS, Boston: May I say that the subject of sporotrichosis always interests me, because I think the first case of sporotrichosis in this state was reported from the Massachusetts General Hospital by Dr. J. H. Blaisdell (The First Case of Sporotrichosis in New England, *Boston M. & S. J.* **176:**811, 1917). I had been much interested in the many reports in the French literature of the different forms of sporotrichosis in France and wondered why they were not seen here. This patient had the characteristics of sporotrichosis leading to a tentative clinical diagnosis, and organisms were found in the smears which, to my uninitiated eye, seemed to point in that direction. When smears were sent to the laboratory, the report promptly came back "negative." Then I had the impertinence to plant some of the material on Sabouraud's mediums and incubated it at room temperature instead of in the incubator, and I promptly got positive results. The trouble in the laboratory had been that the cultures had been kept in an incubator. Of course, all this was a number of years ago.

Anaerobic Streptococcic Ulcer. Presented by DR. C. GUY LANE, Boston.

This woman, aged 52, had "scrofula" at the age of 12 years. In 1917 the Wassermann reaction was weakly positive, but repeated tests have given persistently negative results. She has had infectious arthritis for thirty-four years. She has 1 sister who is arthritic, but there is no other pertinent familial history.

One year ago last June there appeared on one breast a small "pimple," which the patient described as blue. This gradually enlarged, keeping its bluish appearance. The inside seemed full of "pus," and it finally involved a large part of the lateral border of the breast. It healed under treatment in two or three months. There were a similar, smaller lesion on the right breast and another on the right buttock. She has a large scar on the left breast and a small one on the right breast. Similar, smaller lesions have appeared on the elbows, buttocks and right hand. There are two types of lesions: small flat red spots which appear suddenly and small pimples which become raised blue nodules. The lesions are only moderately painful. The present lesion is of two weeks' duration.

On the right internal malleolus is a raised lesion about 1½ inches (3.8 cm.) in diameter, surrounded by an area of erythema. It is bluish with a necrotic center and is covered by paper-thin epidermis.

Boric acid compresses have been applied.

DISCUSSION

DR. J. L. GRUND, Boston: This picture closely resembles that in a number of cases described this week by M. H. Goodman, of Baltimore (Chronic Streptococcic Ulcer of the Skin, *J. A. M. A.* **111**:1427 [Oct. 15] 1938), in which he obtained excellent results with sulfanilamide given internally. I believe a more rational form of treatment and one not so drastic, namely, application of sulfanilamide powder incorporated in boric acid ointment, might have good results.

DR. BERNARD APPEL, Boston: I first saw this patient one year ago, when she had the active ulcerated lesion on the left breast. Microscopic examination of the edge of the active portion of this ulcer showed simple inflammation, and the lesions healed promptly—considering the extent of the ulceration—with frequent applications of solution of sodium perborate followed by an application of allantoin ointment. It resisted treatment with methylrosaniline (gentian violet). The lesions on the buttocks and outer parts of the thighs at that time were grouped firm vesicles on an inflamed base, some of which were crusted; the picture was suggestive of dermatitis herpetiformis.

I agree with the diagnosis of phagedenic ulcers.

Arsenical Keratoses with Carcinomatous Changes. Presented by DR. MILDRED L. RYAN, Brockton, Mass.

This man, aged 52, a hen plucker, has had "stomach trouble" for twenty years, for which he has taken arsenicals in the past twelve years. He began to have cutaneous lesions six years ago. Some have come and gone, but in recent years they have been persistent. Four years ago the top of the right ear began to ulcerate, and a lesion appeared on the left side of the chest which has persisted and grown. The right ear shows an ulcerated crater 1.8 cm. in diameter, involving the entire thickness of the ear down to the cartilage. The border is slightly raised and indurated. Just to the left of the center of the sternum is a 2 by 3 cm. lobulated granulomatous area elevated 1 cm. Numerous keratoses are scattered over the trunk and extremities, and there are keratotic papules on the palms and soles.

The microscopic examination showed basal cell carcinoma.

DISCUSSION

DR. E. LAWRENCE OLIVER, Boston: The lesions on the back, which are slightly depressed and reddish and smooth in some instances, are characteristic of arsenical keratosis. I have seen several that have looked almost exactly like these. The palmar lesions are characteristic.

DR. WILLIAM P. BOARDMAN, Boston: It seems to me that the lesions on the body, appearing several years after those on the palm, were not connected with them. The lesions on the back, of which Dr. Oliver spoke, seemed to me to be typical of a slow growing superficial type of basal cell epithelioma. I could see no keratotic lesions on the body resembling the typical arsenical keratoses on the palms.

DR. J. H. SWARTZ, Boston: I think the pathologic slide will answer Dr. Boardman's question, because it showed no evidence of epithelioma. A slide of one of the lesions from the back showed no evidence of epithelioma but did show a suggestion of Bowen's disease.

DR. MILDRED L. RYAN, Brockton, Mass.: That man had a granulomatous tumor on the chest when I first saw him. It proved to be basal cell epithelioma

when it was removed. I think the section that Dr. Swartz is discussing was made from an ulcerated lesion on the ear, which clinically appeared to be epithelioma but histologically showed no evidence substantiating such a diagnosis. I believe the section was made from the normal tissue rather than the epithelioma.

DR. ARTHUR M. GREENWOOD, Boston: It seems to me a mistake is made in these cases when a diagnosis of Bowen's disease is made. Bowen's disease presents an entirely different picture, and it is a much more heaped-up tumor, uglier looking than these.

Adenoma Sebaceum. Presented by DR. C. GUY LANE, Boston.

This man, aged 30, a foundry worker, states that red papular lesions appeared on the nose and chin twenty years ago. They are red, fleshy, papular and single or grouped, on the nose, adjacent areas of the cheeks, upper lip and chin, and have always been confined to the center of the face. The condition has seemed to improve in the last few years.

Microscopic examination showed a picture consistent with adenoma sebaceum.

DISCUSSION

DR. E. LAWRENCE OLIVER, Boston: I should like to ask if there is any record in the history of this man's mentality and how many years he went to school. I think in a great many cases of adenoma sebaceum there is a certain amount of feeblemindedness.

DR. L. F. RAY, Boston (by invitation): Mentally he is perfectly normal. I think he finished grammar school.

DR. JOHN GODWIN DOWNING, Boston: This man works in a foundry and is exposed to intense heat. He states that since he has been doing this work his cutaneous eruption has been much worse. This case typifies the care which should be used in selecting workers for certain occupations, for this work will accentuate the eruption on this man's face, and if it becomes uncomfortable he can claim compensation for aggravation of a preexisting facial disease.

DR. MAURICE J. STRAUSS, New Haven, Conn.: I do not wish to disagree with the clinical diagnosis, but I do not see how it can be justified with the biopsy report of chronic inflammatory tissue. I did not see a slide, but if this biopsy report is correct, I question whether the specimen was taken from the proper place.

DR. J. H. SWARTZ, Boston: I think the slide is consistent with adenoma sebaceum.

Arsenical Keratoses. Presented by DR. C. GUY LANE, Boston.

This man, aged 67, has had a dermatosis on the body, palms and soles for ten years. Ten years ago he used a medicine containing arsenic, and at that time the first lesion on the hand appeared. Since then lesions have appeared off and on, on the body, palms and soles. In the past eight months a large crop of lesions has appeared. They vary from heaped-up sclerotic plaques of different sizes to less sclerotic ones with a nodular border beneath the crust and include smaller wartlike lesions on the body, which bleed easily.

Treatment consisting of roentgen irradiation, administration of sodium thiosulfate intravenously and fulguration has been followed by some improvement.

DISCUSSION

DR. E. LAWRENCE OLIVER, Boston: The clinical evidence is that the patient had taken arsenic, whether he had a history of it or not. The condition is characteristic of arsenical keratoses, which can be produced, in my opinion, by nothing but arsenic.

DR. ARTHUR M. GREENWOOD, Boston: I think the disease regresses if sodium thiosulfate is given. A young man under my care has been taking sodium thio-

sulfate off and on for two or three years, and he shows marked regression. The palms are almost entirely clear.

DR. BERNARD APPEL, Boston: Apropos of the use of sodium thiosulfate, it seems to me that there might be some rationale also to the use of sodium thiosulfate in the form of fairly concentrated soaks, to be applied externally to the hands and feet. E. D. Osborne (Microchemical Studies of Arsenic in Arsenical Pigmentation and Keratoses, ARCH. DERMAT. & SYPH. **12**:773 [Dec.] 1925) showed definitely a deposit of arsenical amorphous granules in the skin; it seems to me that if there is any beneficial chemical reaction from the use of sodium thiosulfate, it might be of advantage to use it this way. I used it for an elderly patient in whom the taking of solution of potassium arsenite over a great number of years for psoriasis had produced several shallow painful ulcerations on the soles at the sites of arsenical keratoses; these improved rapidly with this treatment.

DR. E. LAWRENCE OLIVER, Boston: I should like to ask what amount of solution of potassium arsenite would be considered safe to give.

DR. BERNARD APPEL, Boston: I saw a woman in whom arsenical keratoses developed after only three weeks' ingestion of solution of potassium arsenite. She said she had never taken any medicine before that she could remember, and at the end of three weeks she began to show arsenical keratoses. She took no dose over 10 drops. If her history was correct, certainly the manifestation was remarkable. I imagine thousands of persons take arsenicals over a period of years and do not have these reactions; certain patients seem to have a predilection for them.

Sarcoma Cutis. Presented by DR. JOSEPH GOODMAN, Boston.

This man, aged 55, in January 1938 noticed a small rounded "lump" on the extensor surface of the right elbow, which grew to 8 mm. in diameter and bled easily, finally falling off in two or three months. It was pinkish gray and projected several millimeters from the surface of the skin. About this time a new lesion appeared near the original one, and later others appeared at the same site. Seven months after the onset the site showed many hard reddish nodules varying from 1 to 8 mm. in diameter; the larger ones are now crusted and bleed on removal of the crust. At this time the right epitrochlear node measures 0.5 cm. in diameter, and there are several palpable nodes in the homolateral axilla.

Microscopic examination showed neurofibrosarcoma.

Acne Varioliformis. Presented by DR. G. MARSHALL CRAWFORD, Boston.

This man, aged 35, a mechanic, has had a dermatosis for fifteen years on the scalp and over the sternum. The lesions, which came out in crops, have never completely cleared. The incidence was not seasonal or occupational, and the family history is irrelevant. The lesions are in all stages from red papules to healed superficial scars, and are rather uniform in size, being from 5 to 8 mm. in diameter.

The microscopic picture was consistent with acne varioliformis.

The treatment has consisted of injections of staphylococcus toxoid and ointment containing 6 per cent sulfur and 6 per cent salicylic acid. He is responding well to this therapy.

DISCUSSION

DR. J. H. SWARTZ, Boston: I challenge the diagnosis. I think this patient has a streptococcic infection or folliculitis. It seems to pick the hair follicles in the scalp and in the chest but skip those on the face and forehead particularly. I have not seen many slides of acne varioliformis, so I cannot comment on the microscopic picture except that this slide showed nothing more than inflammation around the hair follicles. That is not the pathologic picture of acne varioliformis as I remember it.

DR. G. MARSHALL CRAWFORD, Boston: This case was presented at one of the meetings last year, with the question of the same diagnosis, and one of the members suggested folliculitis rather than acne varioliformis. The fact was brought out that this man was an automobile mechanic who handled a good deal of grease, which would give him a perfect excuse for chronic infections of his hair follicles. However, the forearms, which would perhaps get as much or more grease than any other place, were affected practically none at all. He was observed subsequently for some time, and it was discovered that new lesions developed which were not truly varioliform, but had rather a necrotic center, somewhat of the papulonecrotic type. Another factor is that the scars are relatively uniform in size. Uniformity is more of a characteristic of some of the so-called tuberculids and the acne varioliformis group but is not characteristic of ordinary folliculitis. Also, the pathologic picture is fairly good support for the diagnosis.

DR. BERNARD APPEL, Boston: I should like to concur in the diagnosis of acne varioliformis. The lesions are fairly uniform; they show a classic pocklike scarring over the glabrous skin, particularly over the forehead considerably below the hair line, where they were not necessarily connected with hair follicles.

A Case for Diagnosis (Scleroderma? Tuberculid?). Presented by DR. C. GUY LANE, Boston.

This 3 year old girl for two months has had one lesion on each buttock which started as a small red sore and gradually increased in size, with a fading of the center and a red border remaining. On the left gluteal fold there is an annular lesion with an irregular erythematous slightly raised border. The center is clear. The lesion on the right buttock is similar but smaller.

Laboratory tests showed a mild reaction to a 1:100,000 dilution of tuberculin. Microscopic examination showed no evidence of scleroderma, but the picture was consistent with tuberculid.

DISCUSSION

DR. E. LAWRENCE OLIVER, Boston: I think those lesions strongly suggest granuloma annulare. I suppose that might be considered a tuberculid and thereby made to fit the diagnosis on the history card. I should be interested to know what the biopsy showed.

DR. C. GUY LANE, Boston: When I saw these lesions first, the question of erythema annulare centrifugum was raised, as well as the possibility of localized scleroderma. When one sees them in a good light one is impressed by the faint parchment-like character of the center with a slightly red and perhaps a faint purplish tinge to the periphery. When I saw them the other day for the second time, it seemed to me that they were more the type of superficial morphea.

Favus. Presented by DR. C. GUY LANE, Boston.

In March 1927 this 14 year old school girl had a condition which was diagnosed as favus by positive microscopic examination and culture. Her mother and 2 sisters had a condition similarly diagnosed at the same time. Eleven years later she returns with diffuse punctate erosions of the vertex of the scalp. There is minimal alopecia of this area, with moderately atrophic skin. Scattered through the involved portion of the scalp are many faint yellow crusts.

Microscopic examination and culture showed Achorion schoenleini.

In 1928 mild epilation was produced by oral administration of thallium acetate. In 1931 roentgen irradiation produced 40 to 50 per cent epilation. In 1932, after a recurrence of about 75 per cent of the infection, she was again epilated about 50 to 60 per cent by roentgen rays. She is now receiving inhalations of ethyl iodide.

DISCUSSION

DR. E. LAWRENCE OLIVER, Boston: That child has been going to school, apparently. It is eleven years since this diagnosis was made. I do not know what

the board of health was doing about it, if anything. She has been in the hospital several times and, I imagine, reported several times. It seems to me that child is a menace to the other children in the class at school.

DR. J. H. SWARTZ, Boston: I know of another young lady who is going to high school, who has been in the clinic of the Massachusetts General Hospital and other clinics and also has been my private patient, and the other day she came in and told me she was going to graduate from high school. I asked her if she had been attending, and she said she had not missed a day.

DR. WILLIAM P. BOARDMAN, Boston: I talked with the late Dr. John A. Ceconi, former chief of the school physicians, about ringworm of the scalp. I did not mention favus. It seemed to him, and I agreed with him, that the condition was so chronic that something must be substituted if the patient was kept out of school, and there were not enough affected pupils to justify making special classes. Moreover, they generally played with other children outside school anyway, so he could not see much point in keeping them away from school. Dr. Ceconi made the ruling on ringworm of the scalp that if the child wore a cap in school, sort of a boudoir cap that was changed every day, he could go to school; in fact, they were made to go to school. Of course the cap came off about as often as not and was put on wrong side out a good many times. I do not know how much good it did. At the present time, I think the cap is not even required. It is a great problem to know how to prevent such association, which is just as much outside as inside the schoolroom.

DR. JOHN GODWIN DOWNING, Boston: Children suffering from tinea of the scalp are not prohibited from attending school provided the parents exercise due care to prevent the spread of the disease. The children should wear caps and should avoid intimate contact with other children. As regards fungous lesions on the glabrous skin, these are more responsive to treatment, and children suffering from them are prohibited from attendance at school until the condition is relieved.

DR. C. GUY LANE, Boston: This case is an interesting one from the standpoint of difficulty in treatment. As one goes back over the story, one finds that in the the first place in 1928 mild epilation was produced by oral administration of thallium acetate. In other words, there was not complete epilation. In 1931 there was only 40 to 50 per cent epilation by roentgen irradiation. In 1932 there was a recurrence over 75 per cent of the scalp, according to the record. Roentgen irradiation was repeated, but there was only 50 to 60 per cent epilation on the vertex. I do not think that the condition is particularly resistant. I think the youngster did not have enough roentgen treatment. I think favus is the one type of involvement of the scalp in which pretty close to 100 per cent epilation is required. In other words, I should consistently give a patient with favus 300 roentgens for epilation instead of the 270 or 280 roentgens given to patients with ordinary ringworm. That amount of epilation is necessary in order to clear up favus, plus persistent follow-up in order to be sure of the cure. I do not know about the iodide. Dr. Swartz can tell better how ethyl iodide is working out in cases of favus. If it comes to a matter of treatment to clear up the disease—because of course favus does not clear spontaneously at puberty—shall epilation be done again? How many times can a scalp be epilated? I, frankly, do not know. If anybody has the answer I should like to know. I know that 1 patient has been epilated in the hospital three times, but I did it with considerable trepidation and only after a long period and because there had not been complete epilation before. I do not know whether it can be done more than three times, but I do know that that youngster, whose favus had started much earlier, had had uneven epilations; finally he became old enough to sit still and it was possible to obtain complete epilation. As a matter of fact, I think that youngster became infected again a couple of years later from some other member of the family, and I do not know what happened. I did not examine this patient carefully today, but I should be willing to epilate again if there are no large areas of scarring.

Probably the best method of clearing up the disease is by 95 to 100 per cent epilation. I should like to ask Dr. Swartz what his success has been with ethyl iodide.

DR. J. H. SWARTZ, Boston: I have not had many cases in which I used ethyl iodide—I think about 5 in all. Of those 5, there was definite response in 3, in 2 of which either unsuccessful or incomplete epilation had been done. In the other 2 cases the treatment failed. I do not know why. I imagine success depends on the causative organism. I should suggest a combination of ethyl iodide medication and epilation because the infection is resistant.

DR. FREDERICK S. BURNS, Boston: Only one point about this case that interests me, and that is that the nationality was put down as American. Properly speaking, of course the patient is American—she was born here—but obviously her countenance is Italian, and I questioned her and she told me that her parents were born in Italy. How often does one see favus in the indigenous population? Persons who are born here, not of recently immigrated parents, who have no direct contact with the disease seldom have favus.

DR. J. H. SWARTZ, Boston: In 1923 I reported 4 cases of favus in a family of the third generation (Four Cases of Favus in One Family, *Boston M. & S. J.* **189**:507 [Oct. 11] 1923). The parents and the grandparents were American born; beyond that the ancestry was foreign. I do not know whether there was any direct contact at home with a person with favus. Of course, there must be some contact in order to get infection, but those 4 cases were of third generation Americans.

DR. FREDERICK S. BURNS, Boston: The members probably know that favus is not uncommon in the province of Quebec, Canada, in a certain region, and that there is an endemic focus in Gaspé, in that province. I first became interested in that point because I once employed a French Canadian there in the woods who had favus, and I subsequently found that 11 of his family also had the disease. I spoke to several physicians in Montreal, Canada, who told me that they frequently saw favus in French Canadians, invariably from Gaspé, and that apparently the disease has been endemic there for generations and generations.

Kaposi's Sarcoma. Presented by DR. C. GUY LANE, Boston.

This woman, aged 52, first noticed a small black and blue mark on the inside of the midportion of the left calf six months before she came to the hospital. This area gradually enlarged, and with its enlargement she began to have similar areas over the entire leg. Three months later she noticed a bluish discoloration of the right sole. This became more distinct, and soon the entire foot began to swell. The three middle toes became blue and swollen. One month ago the left foot began to swell, and one week later the sole became discolored and the toes underwent the same change. The feet are moderately painful. The lesions are blue-black; some are flat, but the majority are raised. There are several pinpoint-sized lesions and brown-black raised plaques involving the left calf and the arches of the feet. The toes are discolored and involved by edema which includes the feet.

Microscopic examination showed a picture consistent with Kaposi's sarcoma. The patient is improving under roentgen treatment.

Iododerma Superimposed on Old Monilial Infection. Presented by DR. BERNARD APPEL, Boston.

This woman, aged 45, has lesions on the lower third of her left leg. Lesions appeared on both legs twelve years ago. They cleared on the right leg under applications of an ointment of unknown composition, leaving smooth scars. They have continued on the left leg, and although at first they improved with potassium permanganate soaks and ultraviolet irradiation, they are now again breaking down.

She has been taking a cough medicine containing iodides for four years. There is a large area of erythema on the lower third of the left leg, with numerous raised pustules and crusted lesions. There is also an elongated dry pigmented patch on the lateral aspect of the leg.

Monilia was found on a direct smear in December 1937. Microscopic examination showed chronic inflammation.

Granuloma Inguinale. Presented by DR. WILLIAM P. BOARDMAN, Boston.

This Negro, aged 28, a truck driver, six months ago had a small ulcer on the scrotum, which gradually spread so that at present it involves the penis, scrotum and perineum. The lesion is granulating and fungating and extends back to the rectum. A large firm mass about 6 cm. in diameter involves the penile shaft.

The Hinton reaction of the blood was positive on two occasions. Smears and cultures showed staphylococci and streptococci. Microscopic examination showed acute and chronic nonspecific inflammation. Donovan bodies were not seen. The Frei test was negative. There was no improvement after three doses of neoarsphenamine but great improvement after nine intravenous injections of antimony and potassium tartrate.

DISCUSSION

DR. MAURICE J. STRAUSS, New Haven, Conn.: I should like to agree with the diagnosis of granuloma inguinale. Apparently the only question in this case lies between granuloma inguinale and lymphogranuloma venereum. I am told that the lesion originally was a large granulating ulcer, which healed fairly promptly when the patient was given antimony and potassium tartrate intravenously. Lymphogranuloma venereum does not heal under the influence of that preparation. The Frei test was reported as repeatedly negative, and I have confidence in the specificity of that test. It is not always easy to find Donovan bodies, so in spite of the fact that these were not found, I agree with the diagnosis of granuloma inguinale.

DR. WILLIAM P. BOARDMAN, Boston: Has anybody any suggestion as to the treatment? As far as I can see, the only thing is surgical amputation of the penis after the lesions have healed. The whole picture has changed since the injections of antimony and potassium tartrate. Where the scars are was an area of granulations, and after the injections these have entirely healed. My diagnosis has been confirmed by the negative Frei test and by the results of treatment. Donovan bodies have never been found, despite a careful search of the smear and the section.

DR. JOHN GODWIN DOWNING, Boston: I disagree with the diagnosis of granuloma inguinale. I believe that this Negro has lymphangitis of the penis and scrotum and that the surgeon will find several periurethral sinuses. The white translucent appearance which now simulates granuloma inguinale is due to the formation of scar tissue.

Pityriasis Lichenoides et Varioliformis (Habermann). Presented by DR. C. GUY LANE, Boston.

This girl, aged 19, has a rash which developed twelve days ago on her abdomen and spread rapidly to the entire trunk. It is not itchy. The lesions are maculopapular and papular. Many of the latter type have necrotic centers and are hemorrhagic and crusted. She has been taking thyroid and some tablets of unknown content.

The Hinton reaction of the blood was negative.

DISCUSSION

DR. G. MARSHALL CRAWFORD, Boston: I should like to know whether that disease is known to occur in the female.

DR. C. GUY LANE, Boston: The disease does occur in the female.

DR. BERNARD APPEL, Boston: I concur in this diagnosis. The picture seems to be typical of that condition and resembles that in a case I presented at a meeting of this society about three years ago. The nonitchy papular and crusted discrete lesions are characteristic.

Multiple Basal Cell Epitheliomas. Presented by DR. WILLIAM P. BOARDMAN, Boston.

This patient, a woman of 70, was first seen in the clinic on Jan. 11, 1910, at which time a diagnosis of epithelioma of the left side of her nose was made. This lesion had been present for about fifteen years. Since that time many new lesions have appeared at irregular intervals, so that now there are multiple epitheliomas of the face and neck, widely scattered, with destruction of the tip of the nose.

DISCUSSION

DR. WILLIAM P. BOARDMAN, Boston: I am presenting this case merely to illustrate how long the condition sometimes runs. The patient remarked today that Dr. White, whom she saw here, used to treat her and his father treated her before that. The process must have been going on for many years, and yet the only thing that bothers her much now is the deformity of the nose. She is anxious to have something done about this, and a plastic operation has been seriously considered in spite of her age.

DR. BERNARD APPEL, Boston: I recently reviewed the records of the Boston City Hospital and counted the number of times that she had received treatment with radium. It totaled up to what I think is rather an astounding figure: 225 treatments with radium. I should like to hear somebody's opinion as to the advisability of a plastic operation on the nose.

DR. C. GUY LANE, Boston: I think that question ought to be answered by a plastic surgeon, whether he is willing to take the risk, whether he thinks she will stand that. I do not think the dermatologist should answer that.

DR. ARTHUR M. GREENWOOD, Boston: Why should she not have a plastic operation? I do not see any contraindication.

FREDERICK S. BURNS, M.D., *President*

Boston, Dec. 14, 1938

BERNARD APPEL, M.D., *Secretary*

Purpura Simplex. Presented by DR. EDWARD ARTHUR LAFRENIERE, Arlington, Mass.

This 16 year old girl was first seen in June 1938, with a rash which had been present a year, beginning on her right thigh and gradually spreading to the leg. Studies of the blood were made, but the patient did not return to the hospital until November 1938. During that time there was no change in the condition. At the present time the lesions are not so prominent. There are purpuric and pigmented lesions of various sizes on the medial side of the right thigh and calf. They run along the course of the saphenous vein and are red in the center and rust colored at the periphery. They measure from 4 to 6 cm. in length and from 5 to 7 cm. in width.

On June 13, 1938, the hemoglobin concentration was 80 per cent; the white blood cell count, 7,700, and the red blood cell count, 4,580,000. The differential count showed 44 per cent mature forms, 1 per cent young forms, 41 per cent

lymphocytes, 8 per cent eosinophils and 6 per cent transitional forms. The bleeding time was two minutes and the clotting time two and one-half minutes. On December 2 the hemoglobin concentration was 90 per cent; the white blood cell count, 7,100, and the red blood cell count, 5,200,000. The differential count showed 56 per cent polymorphonuclears, 1 per cent young forms, 29 per cent lymphocytes, 5 per cent eosinophils, 8 per cent transitional forms and 1 per cent basophils. The platelet count was 356,000. The bleeding and the clotting time were normal.

Microscopic examination showed some cellular infiltration.

DISCUSSION

DR. EDWARD ARTHUR LAFRENIERE, Arlington, Mass.: The peculiar aspect of this case is that the lesions are asymmetric. There is no history of medication. Six months ago the hemoglobin concentration was 80 per cent and now it is 90 per cent; the red blood cell count was 4,000,000 and now it is 5,000,000, and the white blood cell count has decreased by 600. That is not unusual, but the platelet count has increased from normal to 356,000. The patient is getting on well without any treatment.

DR. BERNARD APPEL, Boston: It has occurred to me that the distribution is remarkably like the anatomic distribution of the internal saphenous vein, and I wonder whether there might be any relation between that peculiarity and some sort of stasis of the small veins which act as tributaries to the saphenous vein.

DR. C. GUY LANE, Boston: In the only other case of unilateral purpura which I have observed the causation was entirely different. The disease occurred in a young woman at the clinic of the Massachusetts General Hospital shortly after she had had an intravenous injection of neoarsphenamine. She had distinct unilateral purpuric areas along the inner side of the arm. I thought the manifestation was extremely unusual, but I found that it had been reported before, shortly after intravenous arsphenamine therapy. It would seem reasonable at least to regard among the causes of unilateral purpura a bite or some mild infection on that particular foot, which would account for the condition of the vessels in that particular area.

DR. WALTER T. GARFIELD, Boston: It seems rather interesting that these lesions have existed for eight and one-half months. The patient told me that they were the same ones that he had in the beginning. It seems to me that in eight months simple purpura ought to have made some change. Even if she had new lesions the old ones should have changed in that time.

DR. J. H. SWARTZ, Boston: I do not know whether Majocchi's disease occurs unilaterally. I see no reason why it cannot. Some of the active lesions show only evidence of pigmentation. The slide showed dilatation of the vessels with an inflammatory process surrounding them and extending to the vessel wall. That is, as I understand it, not inconsistent at least with Majocchi's disease. I should offer that as a possible diagnosis.

Congenital Syphilis. Presented by DR. WILLIAM P. BOARDMAN, Boston.

This 18 year old boy is one of identical twins whose father and mother are being treated for latent syphilis. He reported to the Boston City Hospital clinic on July 1, 1938. He had a positive Hinton reaction. Physical examination revealed prominent parietal bosses, internal strabismus, myopia and chorioretinitis. Mental examination showed mental deficiency on the imbecile level, without psychosis. Roentgenograms of the long bones showed no abnormalities. The spinal fluid showed albumin, 2 plus; globulin, 1 plus; the colloidal gold curve, 000000; 1 cell; the Davies, Hinton and Wassermann reactions, negative, and the total protein, 56 mg. per hundred cubic centimeters. He is receiving neoarsphenamine and bismuth medication.

A Case for Discussion (Dissimilar Reaction in Identical Twins). Presented by DR. WILLIAM P. BOARDMAN, Boston.

This boy is the twin brother of the patient just presented. He reported to the Boston City Hospital clinic on July 1, 1938. The Hinton reaction was negative. Physical examination revealed prominent parietal bosses, internal strabismus and myopia. Roentgenograms of the long bones showed no abnormality. Mental examination showed mental deficiency on the imbecile level, without psychosis. The spinal fluid showed no globulin; the colloidal gold curve, 000000; 2 cells; the total protein, 36 mg. per hundred cubic centimeters, and the Davies, Hinton and Wassermann reactions of the blood, negative.

DISCUSSION OF CASES OF DR. BOARDMAN

DR. AUSTIN W. CHEEVER, Boston: I think it is extremely interesting, if syphilis can really be ruled out in the second case, as I think it can, that one identical twin should have congenital syphilis and the other one not. There are a few cases reported of syphilis in only one twin, though not always cases of identical twins. U. J. Wile and D. G. Welton reported an interesting case (*Am. J. Syph., Gonor. & Ven. Dis.* **22**:544 [Sept.] 1938) and worked it up extremely carefully. One particular point was that the twin with congenital syphilis was much smaller in many measurements than the other one, and I should think it would be interesting to have some studies made of this pair along that same line. I have no idea of the mechanism by which 1 identical twin can have the disease and the other not.

DR. G. MARSHALL CRAWFORD, Boston: Is it not possible that in 1 of these twins there has been a spontaneous cure of the syphilis, which has not been attained in the other? In some cases of acquired syphilis the serum becomes negative. There is no reason why that cannot happen in a case of congenital syphilis.

DR. FRANCIS M. THURMON, Boston: The serologically normal identical twin showed central notching of the upper central incisors; this, I think, is evidence to support the suggestion of Dr. Crawford.

DR. AUSTIN W. CHEEVER, Boston: It is not my understanding that either strabismus or mental deficiency is likely to have anything to do with congenital syphilis, and while it is possible that this patient has burned-out syphilis, it is rather unusual that congenital syphilis will reach that point at any such age as the patient's, at least as regards the Hinton test. With the Wassermann test such a finding would be not at all surprising.

DR. EDWARD ARTHUR LAFRENIERE, Arlington, Mass.: Is it not possible that with more sensitive blood tests both twins would have a positive reaction with all those signs of congenital syphilis? Years ago only the Wassermann test was available; then came the Kahn, and now there is the Hinton, each test more sensitive than the preceding one. As these blood tests are based on a certain amount of reagin in the blood, it is possible that the blood of one of the twins contains an amount of reagin below the percentage necessary to give a positive reaction. The discovery of a more sensitive test in the future may eliminate such peculiar problems.

DR. FRANCIS M. THURMON, Boston: So far as the sensitivity of these tests is concerned, it would be impracticable to increase the sensitivity and not maintain specificity. One suggestion I should like to make is that a special titration be done with the Hinton test because the one or the two tube test as done now will in approximately once in five hundred times give a negative reaction, yet on the same serum, when the technician runs a ten tube test with the varying dilutions of serum, a true positive reaction may be obtained with two or more of these dilutions. I think with a special titration the Hinton test might be positive.

A Case for Diagnosis (Dermatitis of Fingers). Presented by Dr. Francis P. McCarthy, Boston.

This patient, a woman aged 24, was troubled with hangnails more than five years ago and later by frequent infections of the distal phalanges. At the onset and for two and one-half years thereafter, she had "lamp treatments," with but temporary improvement. Recently salves have been used, but the condition has not improved. There is atrophy of the tips of the fingers with scaling, beneath which is a dry red base. The nails are unaffected, and the tissue at the base is erythematous, firm and elevated. Telangiectasia is present in scattered areas.

Laboratory tests showed a hemoglobin concentration of 70 per cent, a red blood cell count of 4,400,000 and a white blood cell count of 16,400.

DISCUSSION

Dr. C. Guy Lane, Boston: I was impressed with the erythema on the backs of the fingers and at the base of the nails, where one can see dilated vessels in which perhaps with the lens in good light one could make out capillary loops, a condition such as I have seen in only 2 or 3 cases of disseminate lupus erythematosus. I do not remember that in any of these cases the disease went on to ulceration. I am unable to explain this ulceration except from lowering of resistance owing to therapy or infection. I thought of Hallopeau's disease; yet there are none of the changes in the nails usually associated with acrodermatitis. There are changes near the peripheral attachment of the nails which suggest psoriasis. The case is most interesting and ought to be followed and reported on later.

Dr. J. L. Grund, Boston: Since this patient has received only ultraviolet radiation, given by Dr. Garfield, the possibility of roentgen dermatitis can be dismissed. In view of the facts that the lesions have been mainly confined to the tips of the fingers, that they first appeared as vesicles and pustules and that they have persisted in the form of low grade ulcerations, I suggest the diagnosis of chronic acrodermatitis of Hallopeau.

Dr. Walter T. Garfield, Boston: I saw the patient a number of years ago, when she had definite psoriasis of the face, elbows and scalp and what looked to me like psoriasis of the nails. The paronychia was definitely pustular, and the lesions extended to the second joint on the fingers. There were also changes in the nails consistent with psoriasis. The Wassermann reaction was negative. I gave her some injections of a bismuth preparation and some ultraviolet radiation. The psoriatic condition cleared, and the fingers were much better when she stopped coming to me. The pustular condition had practically subsided. She says she has some pustular lesions occasionally. I thought the whole picture might be psoriasis, but I was not sure about the atrophic condition. She has never had roentgen or radium treatment.

Dr. E. Lawrence Oliver, Boston: It seems to me that there is a decided vasomotor disturbance in this case. The lesions on the legs look much like those of folliclis seen on the arms, and I think that sort of thing is more likely to occur with such a disturbance. She gives a history of her fingers becoming purple, a manifestation I have seen in some cases of Raynaud's disease, and I think the pustular condition of the finger tips is rather characteristic of Raynaud's disease.

Dr. Francis M. Thurmon, Boston: I saw this girl at the Boston Dispensary about five years ago, when she had her first attack. At that time she was hospitalized for about two weeks. She had a typical erythematous eruption on the nose and malar areas, extending to the jaws and the lobes of the ears, in addition to disseminated lesions of the type sometimes seen in acute leukosis or hemangiosarcoma. Treatment with sodium gold thiosulfate produced clearing. I have not seen her since then.

DR. J. H. SWARTZ, Boston: She said she had had pustules, but on close questioning she says she is not sure they were pustules. She says they contained fluid. There is definite atrophy of the fingers. I should suggest tests for sensory disturbance to rule out syringomyelia.

DR. WILLIAM DAMESHEK, Boston (by invitation): I did not see this patient, but I am wondering whether the diagnoses suggested, acute disseminated lupus erythematosus and Raynaud's disease, might not be brought together. Disseminated lupus is considered by many to be a disease affecting the terminal blood vessels. The description sounds much like Raynaud's disease in some of the cases I have observed, associated with scleroderma and atrophy of the terminal phalanges. If lupus erythematosus is a disease of the blood vessels, it is possible that a severe vascular disturbance of the fingers with what looks like scleroderma with pustules is present.

NOTE.—A subsequent history indicates that there was no exposure to roentgen rays, and the diagnosis of radiodermatitis can be definitely eliminated. The patient received a short course of arsenical therapy (with solution of potassium arsenite), and there was a prompt exacerbation of the lesions with bullous formation and severe pain, which lasted for two weeks after the arsenic had been discontinued. The old psoriatic lesions of the face and scalp also became active at this time. This picture suggests pustular psoriasis rather than acrodermatitis perstans, although it is difficult to differentiate the two conditions.

Cured Hemorrhagic Encephalitis. Syphilis. Presented by DR. WILLIAM P. BOARDMAN, Boston.

This patient, a 17 year old boy, was said to have secondary syphilis on Oct. 7, 1938, and was given three injections of neoarsphenamine (0.15, 0.3 and 0.45 Gm.). Two days after the last injection erythema developed, with a temperature of 103 F. and malaise, which cleared spontaneously. One week after the last injection the patient had a convulsive seizure and lapsed into coma, at which time he had a stiff neck and stiff back. The spinal fluid showed an initial pressure of 350 mm., 180 red blood cells and 40 lymphocytes. A diagnosis of hemorrhagic encephalitis was made. Recovery was uneventful except for the development of a sinus tract in the right buttock.

Laboratory tests showed 85 per cent hemoglobin, 4,750,000 red blood cells and 6,400 white blood cells; the Hinton reaction of the blood and of the spinal fluid were positive.

DISCUSSION

DR. WILLIAM P. BOARDMAN, Boston: The problem of treatment comes up in this case. I think no one would want to give that boy any more arsenic, and where one buttock is pretty well destroyed by scar tissue from the healed sinus, all the injections will have to be given on the good side. One can carry through the treatment for two years with injections of a bismuth preparation alone. C. S. Wright (*J. Chemotherapy* **15**:1 [April] 1938) reported good results in some cases with nothing but bismuth medication, including one of encephalitis following an initial dose of neoarsphenamine. It seems to me that mercurial medication, especially some inunctions, might well be considered in this case. The condition is still in an early stage and needs active treatment.

Generalized Sarcoidosis. Presented by DR. C. GUY LANE, Boston.

This 51 year old woman states that eight years ago a pruritic eruption developed about the hair line on the back of the neck. The eruption spread into the scalp and has since persisted. During the past six months new lesions have appeared on the chest, and deep nodules have been felt by the patient in her arms. The entire scalp is involved in a process consisting of small nodules arranged in linear configuration and covered with moderately thick greasy scales. Flat-topped papules the color of the skin and simulating papules of lichen planus are scat-

tered in rows along the natural creases of the neck and chest. A few firm 4 to 6 cm. brownish nodules are scattered over the face. Along the extensor surfaces of the arms can be palpated firm subcutaneous nodules, averaging 1 to 1.5 cm. in diameter.

Microscopic examination of a cutaneous lesion showed sarcoid. A roentgenogram of the chest showed sarcoid of the lungs, and one small bony cyst of the hand was found by roentgen examination. Solution of potassium arsenite is being used, but it is too early to determine the results.

Sarcoid of Boeck. Presented by DR. BERNARD APPEL, Boston.

This 30 year old Negress has a small circinate elevated lesion on the back of her neck which developed three months ago. Microscopic examination showed it to be sarcoid of Boeck. Since then similar lesions have developed on her neck, chin, abdomen and legs. An antigen made from ground-up biopsy material produced a positive reaction when injected intradermally. She is under treatment for latent syphilis and has just recovered from an arsphenamine purpura. At present she has several small circinate elevated slightly scaly lesions on her chin, neck, abdomen and legs.

Laboratory tests included injection of 1:1,000 dilution of old tuberculin, which gave a positive result. The Hinton reaction of the blood was positive. A roentgenogram of the chest showed pulmonary tuberculosis.

A Case for Diagnosis (Sarcoid of Boeck? Lupus Vulgaris?). Presented by DR. FRANCIS M. THURMON, Boston.

This 51 year old woman has had a lesion beneath the chin since infancy. It has caused no discomfort and has not progressed. The patient has tertiary syphilis. Extensive treatment for syphilis has not influenced the lesion. She is obese and has had hypertension, the blood pressure being about 240 systolic and 130 diastolic since May 1931. She had coronary thrombosis in January 1936. At present there is an area about 4 by 6 inches (10 by 15 cm.) under the chin, which is thickened, raised, dry, scaling and erythematous and through which numerous nodules have coalesced to form a large plaque. There are no apple jelly nodules. There is little or no scarring or destruction of tissue. However, in December 1937 diascopic examination showed numerous apple jelly nodules. At that time a diagnosis of lupus vulgaris was made.

Microscopic examination on Oct. 14, 1938, showed Boeck's sarcoid of the skin.

From Sept. 13, 1929, to March 28, 1936, she received arsphenamine, neoarsphenamine and a bismuth preparation. In April 1930 a postarsphenamine hepatitis, icterus and dermatitis developed.

DISCUSSION OF TWO CASES

DR. J. H. SWARTZ, Boston: I suggest a diagnosis of lupus vulgaris rather than sarcoid. There were typical yellowish itchy apple jelly nodules, with destruction approximately in the center, a picture consistent with lupus vulgaris.

DR. E. LAWRENCE OLIVER, Boston: I am rather in favor of lupus vulgaris.

DR. WILLIAM P. BOARDMAN, Boston: I think the case is remarkable. The woman states emphatically that she has had the lesion as long as she can remember, and it certainly has the appearance of lupus vulgaris. The nodules today look as if they were only a few months or a few years old at the most. I do not recall seeing lupus vulgaris of fifty-one years' duration without more scarring.

DR. JESSE E. EDWARDS, Boston (by invitation): The case with which I am concerned and have had contact is that of the 30 year old Negress. The little that I know about sarcoid comes largely through my association with Dr. D. A. Nickerson. The cause of sarcoid has interested many physicians and is still the subject of some controversy. Many consider the etiologic agent to be the tubercle bacillus. The work that has been done in the pathologic laboratory largely by Dr. Nickerson has, I think, pointed definitely to a virus as the cause.

The histologic picture of sarcoid is similar to that of tuberculosis. When the diagnosis of sarcoid is considered there should be no caseation and no tubercle bacilli, either by direct examination of the stained section or by inoculation of macerated skin into guinea pigs.

Another interesting feature of sarcoid is that biopsy material from a typical lesion, macerated, diluted with saline and inactivated, will produce a positive reaction when used in cutaneous tests of persons having this disease; persons who are considered well will not react to the test. Incidentally, a positive reaction in a case of sarcoid has the exact histologic appearance of a primary spontaneous sarcoid.

The picture presented by the 30 year old Negress is rather typical of that in a group of cases, many of which Dr. Nickerson has observed, in which there are two predominant features: (1) the cutaneous lesions, which have a habit of a more or less hit or miss distribution, and (2) pulmonary lesions seen on roentgen examination, which are similar to those of miliary tuberculosis. In several cases incidental roentgenograms of the chest have shown miliary tuberculosis. The peculiarity about these cases is that although miliary tuberculosis is diagnosed on roentgen examination sometimes when they are followed for several years the roentgen picture of miliary tuberculosis persists while good general health is maintained. The only impairment of health presented in most of these cases is perhaps related to some scarring of the lung, i. e., some dyspnea and occasionally scattered rales through the lungs. Another feature of the cases of generalized sarcoid is enlarged lymph nodes, particularly of the mediastinum. Frequently these lymph nodes are not thought to be enlarged unless a lateral roentgenogram of the chest is made. Another feature is that the serum protein is elevated rather universally, which again points, I believe, toward a virus disease, or is at least consistent with a virus disease. In many virus diseases the serum protein is elevated. Another rather striking feature is that the Wassermann reaction of the blood is occasionally positive and at times is considered falsely positive.

No treatment has been curative. Dr. Nickerson treated a few patients with antigenic injections. Some responded to injections of sarcoid antigen. One patient had pulmonary involvement as the outstanding feature, and there was considerable resolution over a period of time. Whether the antigen hastened the resolution one cannot say, because I think some of these patients have spontaneous resolution.

Dr. Nickerson reported a series of 6 cases of generalized sarcoid with autopsy data (*Arch. Path.* **24**:19 [July] 1937). Lesions typical of sarcoid were present in many of the viscera, predominantly the spleen, liver, lungs and lymph nodes. Occasional lesions were present in the heart and the bone marrow.

The prognosis of this condition, from the relatively few cases which Dr. Nickerson and I observed, is, I believe, reasonably good. Of the 6 cases in which autopsy was done there was only 1 in which sarcoid was considered to be the cause of death. In the other 5 cases there was adequate cause of death other than the sarcoid.

Tuberculosis of the Skin. Presented by DR. JOHN GODWIN DOWNING, Boston.

This 29 year old woman has pulmonary tuberculosis, having been in Lakeville State Sanatorium, Middleboro, Mass., from December 1936 to May 1937. A large granulating lesion developed on the right cheek and a similar lesion on her left buttock; both of these were excised after about eight months. Three months ago several translucent nodules 2 to 3 mm. in diameter developed about her external nares. There is a conglomeration of lesions on the septal border of the left external naris. These lesions are light reddish brown and soft.

Microscopic examination showed a tubercle bacillus in one section. The Hinton reaction of the blood was negative.

Tertiary Syphilis with Syphilitic Cirrhosis of the Liver. Presented by Dr. William P. Boardman, Boston.

This 39 year old woman was referred to the dermatologic clinic because of a positive Hinton reaction of the blood. In 1930 at the Massachusetts General Hospital a diagnosis of cirrhosis of the liver was made; in 1932, one of hepatitis and chronic cholecystitis, for which she was operated on; in 1935, one of cirrhosis of the liver, and in 1936, one of cirrhosis of the liver and ascites.

The patient entered the Boston City Hospital seven month ago, complaining of pain in the legs and inability to walk. At that time a physical examination showed the edge of the liver to be 3 fingerbreadths below the costal margin, hard, firm and nontender. There was great tenderness over both tibias. During six weeks at the hospital the patient lost 10½ pounds (4.8 Kg.).

Laboratory tests showed 71 per cent hemoglobin, 3,250,000 red blood cells, some macrocytes, an increased platelet count and 5,800 white blood cells, with a differential count of 20.5 per cent polymorphonuclears, 37 per cent stab cells, 5 per cent eosinophils, 1.5 per cent basophils, 24.5 per cent small lymphocytes, 2.5 per cent large lymphocytes, 4.5 per cent mononuclears, 0.5 per cent young myelocytes, and 4 per cent myelocytes. Three Hinton tests gave negative results; the urine was normal.

Microscopic examination of a cervical lymph node showed hemangioendothelioblastoma, probably metastatic.

Physical examination of the patient at the present time reveals an enlarged tender liver 3 fingerbreadths below the costal margin, an enlarged spleen and tenderness over both tibias. There have been positive Hinton reactions of the blood on three occasions recently. There was no evidence of a recent syphilitic infection. Roentgenograms showed localized periosteal thickening of the upper part of the left tibia.

DISCUSSION

Dr. William Dameshek, Boston (by invitation): This patient has apparently had chronic hepatitis for six years—possibly longer—and only recently the Wassermann and Hinton reactions became positive. She was found to have an enlarged liver, and recent studies have demonstrated all the various clinical and laboratory features of chronic cirrhosis of the liver. The lowered red blood cell count with a macrocytic type of anemia is characteristic. The unusual feature is that a positive serologic reaction has been present on three successive occasions. Does that mean that she has syphilis and syphilitic cirrhosis? Hepatosplenomegaly of chronic syphilis, usually in association with moderate anemia and leukopenia, is not infrequent.

The condition is refractory to therapy. J. H. Stokes studied a number of cases some years ago. He found that persistent antisyphilitic therapy failed to clear up the process. Finally splenectomy was performed in some cases with resultant improvement clinically and serologically. The measure is rather radical, and I doubt whether it is indicated in this particular case.

Another interesting feature is the enlargement of a lymph node, diagnosed as malignant. In some cases of long-standing cirrhosis, cancer of the liver actually develops. One wonders whether the malignant change of the lymph node might not be metastatic, with a condition originating in the liver causing this picture of what is described as hemangioendothelioblastoma.

Dr. William P. Boardman, Boston: There is definite periostitis of the tibias. From the clinical and roentgen appearance, that cannot be explained on any other ground than syphilis. How to explain the three negative Hinton reactions during hospitalization I do not know, but it seems to me that about everything else in the case can be explained by syphilis. She did have an enlarged spleen. That is not mentioned in the hospital record, but it was definitely palpable when she was examined as an outpatient. Whether that is something new I do not know.

As to treatment, I think the results in these cases depend on how much of the process is cirrhosis and how much is gumma. When the predominant, pathologic process has been gumma, I have seen some remarkable results from treatment of syphilis of the liver. There is always some cirrhosis with gumma, and there is always some gummatous involvement with the cirrhosis. I should not be so discouraging about treatment as Stokes was. My feeling would be more like that expressed by J. E. Moore (The Modern Treatment of Syphilis, Springfield, Ill., Charles C. Thomas, Publisher, 1933, p. 304) on the subject: Treatment should be instituted, and if no results appear in a few months, there is little point in pushing it further. In some cases, however, involvement that looks to be mostly cirrhotic turns out to be more gummatous. Treatment should be rather mild at first on account of the possibility of a Herxheimer reaction or a therapeutic paradox; after the start it should be pushed fairly vigorously.

Dr. Francis M. Thurmon, Boston: This condition is typical hepatosplenomegaly due to syphilis, the type in which one attack of ascites is followed by two or more attacks and then death. At the time of autopsy the liver will be small, typical of the scarred fibrous liver of cirrhosis. I have followed patients like this in the clinic at the Boston Dispensary and have seen them come to autopsy. Some of them go through as many as five attacks of ascites, associated with malaise and fever and prostration, which last anywhere from six weeks to three months. Sometimes there are periods of two or three years between attacks, but eventually one of them will carry the patient off, and treatment does not seem to influence the progress of the disease.

Dr. E. Lawrence Oliver, Boston: I do not think the value of potassium iodide should be forgotten in these cases. I think sometimes that preparation gives better results than more modern means of treating syphilis. Although, of course, I should not withhold the modern treatment, I believe potassium iodide should be given as well.

Dr. J. L. Grund, Boston: I should like to say in connection with Dr. Oliver's statement that Dr. C. Morton Smith depended almost entirely on iodide in treating this disease.

Scleroderma. Presented by Dr. William P. Boardman, Boston.

Tinea Corporis (Trichophyton Purpureum). Moniliasis of Feet. Ichthyosis. Presented by Dr. C. Guy Lane, Boston.

This 28 year old woman stated that one year ago "athlete's foot" developed, with pruritus and moist sodden skin between the toes. A few weeks later a generalized eruption developed on the body and has persisted. The patient has had ichthyosis since birth. All the interdigital spaces of the feet present areas of moist sodden skin and fissuring. There is mild generalized ichthyosis. On the chest, buttocks, thighs and back are raised red borders with a bilateral polycyclic and geometric pattern.

Cultures of material from the body showed Trichophyton purpureum. Cultures of material from the interdigital webs of the feet showed Monilia albicans. The patient has responded well to ethyl iodide inhalations.

DISCUSSION

Dr. J. H. Swartz, Boston: This condition, I think, is rather rare, not the usual type. Local treatment does not seem to help. The treatment in this particular case has been by inhalations of ethyl iodide. I have not seen the patient for a while, and she shows great improvement. Ordinarily, the condition does not get better spontaneously.

Dr. C. Guy Lane, Boston: An interesting point is that she has always had an ichthyotic skin, and when seen earlier it seemed as if the areas over which the present condition had traveled showed less of the ichthyosis than the skin which had not been affected.

Lupus Erythematosus, with Lesions of the Buccal Mucosa Changing to Epidermoid Carcinoma. Presented by DR. FRANCIS M. THURMON, Boston.

This 23 year old man states that in December 1937 a small red "pimple" developed at the nasofrontal junction. Soon other erythematous macular and papular lesions began to appear, over the nose, forehead, premalar regions, cheeks and sides of the neck posterior to the level of the ear lobes. Under treatment the eruption cleared except for one resistant patch beneath the outer corner of the right eye. Lesions of the buccal mucosa were first noted on Aug. 18, 1938.

At present there is a solitary patch of dry oval scaling slightly elevated lupus erythematosus on an erythematous base, approximately 2 cm. in diameter. Previously, when the facial eruption was more profuse, there were erythematous macular areas which could be blanched under pressure and dry scaling papular oval and circinate lesions partially covered with a thin scale. Their greatest diameters were 3.5 or 4 cm. and their distribution fairly symmetric. The lesions on the buccal mucosa are dull, milky, leukoplakia-like and diffuse, with superficial ulceration opposite the molars. The patient's general health has remained good.

He has improved under treatment with sodium gold thiosulfate, bismuth subsalicylate, calcium gluconate and bismuth oxychloride ointment.

DISCUSSION

DR. FRANCIS M. THURMON, Boston: I have observed only 3 cases, including this one, of lesions on the buccal mucous membrane with discoid lupus erythematosus. In 2 of those cases, if the diagnosis is accepted in this case, I have seen malignant change occur. I presented this case in the hope of some suggestions as to therapy of those lesions which, histologically at least, are becoming malignant—a slow-growing progressive type of malignancy. Should they be treated as though the malignant change was entirely separate from the lupus, or does the lupus influence the type of treatment?

DR. BERNARD APPEL, Boston: I should like to suggest fairly extensive electrocoagulation during anesthesia with procaine hydrochloride for both conditions, even if one has actually degenerated into the other. I had fairly good results in 2 cases of lupus erythematosus with lesions of the buccal mucous membrane. There was a recurrence in 1 instance and none over a period of several years in the second. The interesting thing about my experience with those lesions of the buccal mucosa is that I found them particularly resistant to gold treatment, whereas the lesions on the glabrous skin responded well.

Ehlers-Danlos Syndrome. Presented by DR. FRANCIS M. THURMON, Boston.

This 3 year old boy bleeds easily on slight trauma. His skin heals slowly and with much scarring. The oral mucous membrane is fragile. The skin is generally hyperelastic; the joints are loose, particularly those of the fingers. At times he walks into the sides of buildings. He has suffered from this condition since birth, and it has grown progressively more noticeable. His birth and development were apparently normal. There is no history of syphilis. There is one other normal child in the family.

On trauma the skin pulls apart, bleeds, heals slowly and becomes scarred. There are numerous scars over the frontal bosses and scalp, a thin shiny epithelial repair without keloid formation. The skin is hyperelastic and wrinkles easily, and there is a loss of tone and resiliency. There are vascular nevi on the nose and symmetrically on the anterior surfaces of the lower parts of the legs. The frontal bosses are prominent.

DISCUSSION

DR. CHARLES WILLIAM O'NEILL, Hartford, Conn.: I should like to venture some thoughts on this case and offer for consideration the diagnosis of Ehlers-Danlos syndrome, in which there is a triad of signs, namely, hyperelasticity of

the skin, hyperextensibility of the joints, especially the thumbs, and friability of both the skin and the blood vessels.

In this case there were hyperelasticity of the skin and hyperextensibility of the joints, and while there was no linear solution with resultant linear scarring over the elbow and knee joints and the ankles, there was traumatic scarring of the forehead over the bosses, indicating friability of the skin.

With these three signs I offer for consideration the diagnosis of Ehlers-Danlos syndrome.

DR. FRANCIS M. THURMON, Boston: I think the diagnosis of Ehlers-Danlos syndrome is correct. That was the diagnosis I made originally a week ago, when the patient first came under observation. I think the lack of scarring may be accounted for by the fact that the patient is only 3 years old. Most patients with this disease are much older and have had an opportunity to become scarred. I thought for a time that I might find some retinal changes such as are present in 25 per cent of cases of pseudoxanthoma elastica, but the retinal examination gave entirely negative results in this case.

AMERICAN ACADEMY OF DERMATOLOGY AND SYPHILOLOGY

A. H. CONRAD, M.D., *Chairman*

Clinical Meeting, St. Louis, Nov. 15, 1938

ROY L. KILE, M.D., *Secretary*

Tuberculosis Verrucosa Cutis. Presented from the Barnard Free Skin and Cancer Hospital.

E. G., a white man aged 55, states that an eruption began on his right little finger three years ago and slowly spread across the back of the hand. At times a little pus exudes. There is no history of tuberculosis. The skin on the dorsum of the right hand is atrophic, thin and erythematous. Over the head of the third metacarpal bone is an area about the size of a half dollar, which is slightly demarcated, elevated and brownish red. The central portion is of a verrucous papillary nature. A similar crescentic lesion extending across the dorsum of the wrist is about 1 inch (2.5 cm.) wide.

A roentgenogram of the lungs showed old healed tuberculosis. The histologic picture was typical of tuberculosis.

Lupus Miliaris Disseminatus Faciei et Colli. Presented by DR. JOSEPH GRINDON and DR. JOSEPH GRINDON JR., St. Louis.

S. B., a Negress aged 36, was first seen at the dermatologic clinic of the St. Louis City Hospital No. 2 in October 1934. Four years before she had noted a small patch of thickened skin at the nape of the neck, followed by lesions on the face and extension of the patch on the neck. Since then the lesions on the face have become confluent in many places, and new lesions have appeared elsewhere.

Examination shows patches of raised firm dark red nodules at the mesial canthi and the nares and about the alae nasi and a few discrete small lesions of similar character on the cheeks and forehead. On the dorsum of the neck is a continuous patch 12.5 by 12.5 cm., of the same general character as the lesions on the face and presenting a somewhat nodular surface. On either side of the neck are several narrow linear bands of similar character along natural creases.

General physical and laboratory examinations gave essentially negative results. Histologic study showed irregular acanthosis and spongiosis. Owing to a dense infiltration of the corium, the junction of the epidermis and corium was difficult to define. Throughout the upper and the middle portion of the corium well defined tubercles containing giant cells of the Langhans type and some with central caseation were seen. An extensive infiltrate was present in the upper and middle portion, and in the lower part, a banal infiltrate consisting of lymphocytes.

Erythema Induratum. Presented from the Barnard Free Skin and Cancer Hospital.

E. R., a white woman aged 51, states that eleven years ago a few small lumps appeared on the back of the lower part of each leg. Shortly afterward ulcers formed; these have healed slowly and have a tendency to recur. Roentgen treatments healed the ulcers at one time, and they remained well for some time. Four years ago small nodules again appeared; ulcers formed, and she came to this clinic in October 1935. There was no familial history of tuberculosis, but the patient had undergone excision of some enlarged and suppurating glands of the neck in childhood. There is an irregular discoloration the size of a palm on the posterior and medial surface of lower third of each leg. This has a sharply demarcated border, and the whole is slightly depressed and scarred. There are a few large punched-out ulcers in this area, with dirty granulating bases. The lesion is indurated, and deep nodules may be felt on palpation.

The Wassermann and the Kahn test were negative. A roentgenogram of the heart and lungs was normal, and a determination of blood sugar and urinalysis gave normal results. In the microscopic section a lesion occupying more than one low power field had a central area of necrosis and a surrounding area of infiltrate. This infiltrate was seen to consist of numerous epithelioid cells and lymphocytes and a few giant cells. There was a moderate amount of fibrosis, and the vessels were dilated.

The ulcers healed in a few months of supportive treatment and rest, but the patient complains of severe itching in the scars.

Sarcoid (Angiolupoid Type). Presented from the Barnard Free Skin and Cancer Hospital.

H. G., a white man aged 40, states that an eruption began eight years ago as a small area of thickening of the skin on the left side of the face. This enlarged slowly for five years and then increased rapidly to its present size. About three years ago similar lesions appeared on the neck and on the right arm. The patient's mother died of tuberculosis in 1914, but there was no other case of tuberculosis in the family. The patient had been fairly healthy except for epilepsy, which began at the age of 15. No cause has been found for this, and barbiturates have controlled it for years.

There is a sharply demarcated elevated tumor-like lesion on the left cheek and nose. It extends from the bridge of the nose to the zygoma and from the upper lip to the eye. It is firm and seems to be part of the epidermis; the skin is normally movable over the underlying structures. The surface is dull purplish red and intact and shows telangiectasia, which stops abruptly at the edge of the lesion. There is a similar, smaller lesion on the right arm and one on the neck.

The hemogram was normal and the Kahn reaction negative. A roentgenogram of the chest showed no abnormality. Inoculation of a guinea pig gave negative results. Cutaneous tuberculin tests gave negative results, but there was a slight general reaction to subcutaneous injection of tuberculin. The section was taken from the lesion on the neck. Throughout the middle and lower parts of the corium were scattered definitely localized areas of infiltrate, rich in epithelioid cells and the Langhans type of giant cells, with a moderate amount of lymphocytes and scant necrosis. The presence of dilated vessels in the surrounding tissue and of an occasional vessel within the area of infiltrate was striking.

DISCUSSION OF FOUR CASES

DR. H. E. MICHELSON, Minneapolis: I heartily agree with the diagnosis of a verrucous type of tuberculosis in the first case. All the members probably noticed an exudate of pus and serum. It should be emphasized that verrucous tuberculosis frequently acts like pyoderma until it becomes a settled tuberculous process. Cauterization plus roentgen irradiation is the treatment of choice. It should also be emphasized that verrucous lupus vulgaris and extensive tuberculosis verrucosa acuta are sometimes almost indistinguishable. The distinction probably is only a matter of the depth of the process. However, frank verrucous tuberculosis responds well to treatment, while lupus vulgaris is notoriously resistant. Therefore every effort should be made to establish the identity of the process before proceeding with the treatment.

The second case offers an opportunity for controversy. To me the condition is that type of tuberculosis that various American observers have observed in the American Negro. I should prefer, for the time being, to call this a sarcoid type of tuberculosis in the Negro. There can be no question that the individual lesions might resemble almost any type of cutaneous tuberculosis, but taking the picture as a whole I think it is a rather well established entity.

The third case, to be sure, is one of erythema induratum, and in my way of looking at this condition the circulation, or varicosity, plays an important part not only in the localization of the process but in the treatment. I always use a supportive agent in the form of an Unna cast or an elastoplast bandage, and I feel certain that it assists in the cure of the lesion.

The fourth case offers the observer the privilege of applying a name consistent with his point of view. I prefer to use the word sarcoid for all such conditions, knowing full well that it is not an ideal term. "Angiolupoid" has been in the literature for a long time, is descriptive and brings to the hearer a concrete clinical condition. However, I do not believe that any condition should be so designated before investigation of all the other tissues, such as lungs, bones, glands and tonsils, in which the same pathologic process may be active; when activity is found in tissues besides the skin, one realizes that one is dealing with a generalized disease and not just a morphologic entity in the skin.

DR. W. H. GUY, Pittsburgh: Clinically, the lesion in the first case impresses me as blastomycosis. The infiltrated verrucous lesions at the edges closely simulate verrucous tuberculosis, but according to the history that I obtained, the disease progressed from the original focus on the finger over the dorsum of the hand and the head of the third metacarpal bone, where it has apparently cleared spontaneously, leaving no hypertrophic scarring. Such a course is not characteristic of verrucous tuberculosis during healing. In favor of a diagnosis of tuberculosis is the fact that the patient has pulmonary tuberculosis. On the other hand, I understand from the presenters that originally a diagnosis of blastomycosis was made but on repeated examinations blastomyces were not found; further, I believe I am correct in the assumption that the tubercle bacillus was not seen in the lesion on histologic section. In the absence of conclusive proof of one diagnosis or the other, from a clinical standpoint I should favor a diagnosis of blastomycosis.

DR. JOSEPH GRINDON, St. Louis: The second patient is a Negress with brownish red lesions on the face and the back and sides of the neck, lupus miliaris disseminatus faciei et colli. The section showed a tuberculous structure. Drs. Fred Wise and D. L. Satenstein reported several cases of similar involvement with excellent illustrations in the ARCHIVES (**4**:586 [Nov.] 1921). Three of the patients were Negresses, as this woman is, and the distribution of their lesions was strikingly like that in this case, namely, about the eyelids and in the furrow on the outside of each naris. Two of them, however, had lesions about the lips, which this patient did not have when the photograph was taken but which have since developed. Those patients had no lesions on the neck, which in this patient was the first site involved.

Chromomycosis. Presented from the Barnard Free Skin and Cancer Hospital.

M. S., a white man aged 67, noted a nodule on his right cheek ten years ago at the site of a sulfur burn. It has slowly enlarged since that time. No sensation or discharge is noticed. In the infraorbital area on the right is a discrete elevated pinkish lesion (fig. 1). There is a crust over the center of the lesion, but no discharge or bleeding. The lesion measures 5 by 4 cm., is elevated 2 to 5 mm. and is indurated. Culture of tissue from the area yielded a fungus identified as Phialophora verrucosa.

Histologic section (fig. 2) showed hyperkeratosis and decided acanthosis, with elongated interpapillary processes extending into the hyperplastic papillae. The infiltrate in the corium consisted of numerous lymphocytes, plasma cells, polymorphonuclear leukocytes and epithelial cells. A number of Langhans giant cells were also present. The fungus cells were inside the giant cells.

The lesion has improved remarkably during mixed treatment with mercury bichloride and potassium iodide.

DISCUSSION

DR. FRED D. WEIDMAN, Philadelphia: This case, as far as the location of the lesion is concerned is unique. Dr. C. Guy Lane was the first dermatologist in the United States to observe the micro-organism. In his case, too, the location was unique; the lesion was on the buttock and clinically resembled lupus vulgaris. In all the reported cases, except Dr. Lane's and this St. Louis case, the disease has involved the legs. I take it that the appearance of this lesion is not diagnostic; however, its present appearance is doubtless not that originally presented. As I understand it, the lesion before modification by treatment resembled tuberculosis verrucosa cutis or perhaps blastomycosis. I take it that the diagnosis was made in this case only because pains were taken with laboratory studies, as was done in Dr. Lane's case.

Altogether in the United States there have been only 4 or perhaps 5 reported cases: Dr. Lane's Boston case; the Forth Worth, Texas, case reported by Drs. S. J. Wilson and S. Hulsey (ARCH. DERMAT. & SYPH. **27**:107 [Jan.] 1932), and in which I collaborated in the laboratory work; this case, and 1 or 2 in Durham, N. C. Two or 3 cases have recently been reported from Puerto Rico.

The latest development that I know—and it is pertinent indeed to this case—is the finding by N. F. Conant (*Mycologia* **29**:597, 1937) in Durham, N. C., that a parasite (Cadophora) of the same general kind as P. verrucosa has been found on fresh undressed lumber—spruce and pine. This St. Louis patient gives a history of having had contact with this material. The parasite grows in rather black colonies and is of a kind that is widespread in the world of nature as a saprophyte; to be precise, it belongs to the Hormodendrum group, of which there are numerous varieties. The disease is comparatively common in South America.

DR. MORRIS MOORE, St. Louis: I should like to discuss this case chiefly because, as Dr. Weidman pointed out, the lesion is in an extremely unusual location. I have a number of lantern slides that I should like to present, just to show some of the clinical features, some of the microscopic features and some of the organisms that have been isolated in this case and many South American cases, mostly in São Paulo, Brazil.

The disease was apparently first mentioned by Pedroso in Brazil in 1911. His report, however, was not published until 1920, when with Gomes he reported 4 cases. The first case actually reported was that of Dr. Lane from Boston, in which the lesions occurred on the buttocks of a 19 year old youth. Not only was this the first case published, but it represents the first case of unusual location, since all others reported have occurred on the hands or feet. The organism in this case was identified by Medlar as P. verrucosa.

Clinically, chromomycosis is usually a disease of the hands or feet; it may be papular, nodular, verrucoid or granulomatous, with or without ulceration and abscess formation, and is usually yellowish brown. A typical lesion often presents cauliflower-like growths, some being pedunculated. There is usually no pain or lymphangitis.

Microscopically the picture resembles closely that of tuberculosis, syphilis, blastomycosis, a granuloma or a foreign body reaction. This is particularly evident in the decided hyperkeratosis, the acanthosis and some parakeratosis of the epidermis, owing to the hypertrophic changes in the epidermal cells. In the corium there is marked edema with intense infiltration and fibrosis. This is made apparent by the granulomatous lesions with polymorphonuclear leukocytes, numerous lymphocytes, plasma cells, epithelioid cells, eosinophils, Russell's fuchsin bodies, macrophages, fibroblastic changes, discrete microabscesses and many giant cells of the Langhans or foreign body type. These are often arranged in tubercle-like fashion, confusing the picture with tuberculosis. Within these giant cells or distributed

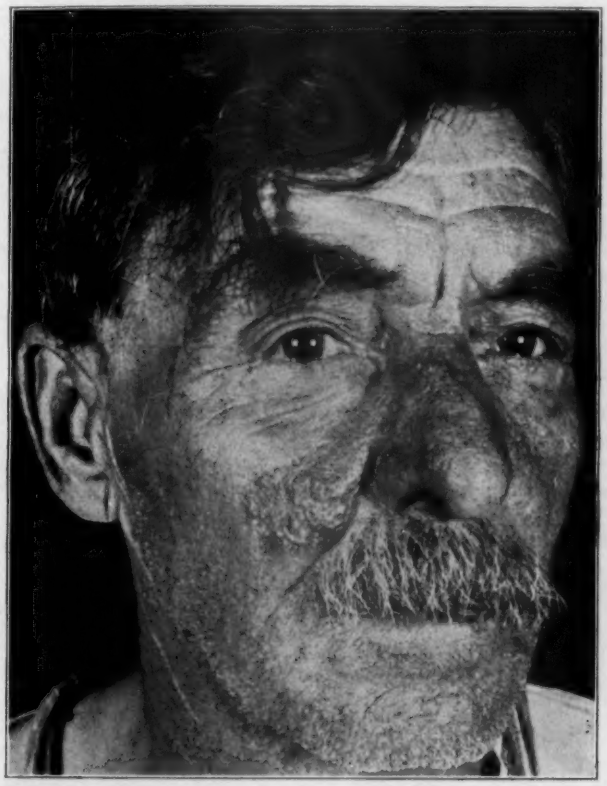


Fig. 1.—Chromomycosis.

freely in the tissue may be seen the multilocular thick-walled brown cells of the fungus P. verrucosa. These cells do not reproduce by budding, but by transverse septum production which forms multilocular cells like mulberry clusters. Accordingly, with the report of F. P. De Almeida and me (*Ann. Missouri Botan. Garden* **23**:543, 1936), the name was changed from chromoblastomycosis, given to the disease by O. da Fonseca and A. E. de Arêa Leão (*Rev. med. cir. d. Brasil* **6**:23, 1930), to chromomycosis.

A number of fungi may produce the disease. These have different morphologic characteristics which seem to relate them to each other in a phylogenetic sequence. The time is too short to permit a lengthy discussion of each, but they may be

briefly listed as we described them: P. verrucosa, Phialophora macrospora, Phialoconidiophora guggenheimia, Phialophora compactu, Hormodendroides pedrosoi, Botrytoides monophora, Hormodendrum langeroni, Hormodendrum chaquensis, Hormodendrum algeriensis, and several other species of each of these genera.

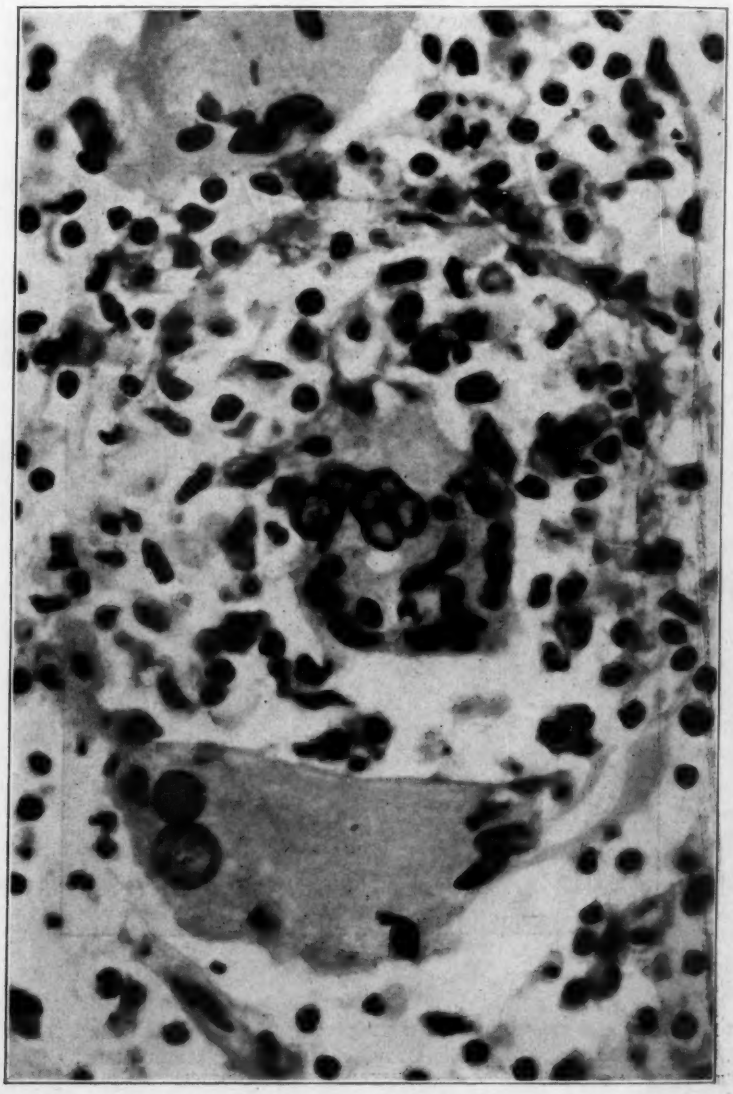


Fig. 2.—Sclerotic fungous cells within giant cells; × 750.

In conclusion may I say, therefore, that this case is the fifth of chromomycosis due to a species of Phialophora and the fourth due to P. verrucosa; it is unique in that the primary lesion occurred on the face and is the second case in which the lesion occurred in some other site than on the extremities.

Generalized Moniliasis. Erythroderma Ichthyosiforme Congenitale. Presented from the Barnard Free Skin and Cancer Hospital.

S. H. and H. H., twin white youths aged 17, present an illness which began at the age of 7 years, when both acquired "athlete's foot." This appeared on the toes and sides of the feet. During the first few years it got well in summer and worse in winter, but for the past five years it has been progressive. The maternal grandmother had a scaly eruption (erythroderma?) on her knees all her life. One sister and 1 brother are well, but an older sister had "athlete's foot" on her hands and feet three years ago for a short time. At the age of 2 or 3 months each boy had a dry red scaly area on the knees. H. H. also had it on the front of the ankles. This proved to be erythroderma ichthyosiforme congenitale. They have had the usual diseases of childhood, but are in good health except for the skin.

Both boys have erythematous scaly patches on both knees. These consist of small follicular papules which measure about 1 by 2 inches (2.5 by 5 cm.) and are all that remain of the erythroderma ichthyosiforme, which had been more extensive in childhood. The feet of both boys present deep white sodden irregular macerated and exfoliating ulcerations involving the thick epidermis. These patches are on the soles, sides of the feet and heels and between and on the toes. The groins are involved, that of S. H. more extensively. Here the skin is dry, superficial and erythematous and covered with thin shiny scales; the involvement extends onto the scrotum and penis. There is hyperhidrosis of both the hands and feet. The exfoliation on the hands is confined mostly to the palms. At one time each boy had a milky white vesicular eruption about the corners of the mouth and on the lips. The tongue and mucous membranes were also covered with a milky white exudation, which could be scraped off. At present in both cases the mouth and lips are free, but the tongue has fissures across the anterior half. The scalp has presented piled-up pustular crusted isolated lesions over the posterior half, accompanied with slight loss of hair in the affected area. Since these lesions have improved the hair has grown back.

The Kahn reaction has always been negative and the hemogram and urinalysis normal. Smears and cultures were made of material from the feet, hands, groin, lips, tongue and scalp, and from each location Monilia albicans was isolated in pure culture. Methylrosaniline (gentian violet) at one time caused the lesions in the mouth to disappear, but they recurred. The preparation was ineffective elsewhere. Roentgen and ultraviolet radiation have been tried at various times with indifferent results. A resorcinol lotion effected a cure on the scalp but no change in the other lesions. Tannic acid was of no benefit. Several ointments have been used with only slight improvement. The boys at times cannot wear shoes and nearly always have difficulty in walking. Itching is always severe, especially at night. An autogenous vaccine was made and has been given only to H. H. He has improved more than S. H.

DISCUSSION

Dr. Richard S. Weiss, St. Louis: These 2 boys and their sister were described by Dr. Norman Tobias and me (Arch. Dermat. & Syph. **12**:182 [Aug.] 1925) with a diagnosis of congenital ichthyosiform erythroderma. This sister is still under our observation and still has the disease. The 2 boys still show lesions of this condition, especially keratotic lesions about the knees and on the front of the ankles. Now there has developed on top of this another condition, which is characterized by deep-seated vesicular lesions on the palms and soles and a rather superficial epidermic process, exactly comparable to the eczema marginatum of the older writers, in the groin. There is also a fungating or "frozen door mat"–like eruption on the buccal mucosa and on the lips.

Our mycologist has found Monilia in scrapings from the mouth. It is true that one can at times get Monilia from normal mouths, from the bowel contents and occasionally from the skin in areas of macerated epidermis; but he also recovered this organism from the deep-seated vesicles on the palms and soles, and I have

considerable confidence in the diagnosis of a superimposed moniliasis on the mucous membranes, in the genitocrural regions and on the hands and feet.

I cannot say that my associates and I have proved that this monilia which we have recovered is the cause of the secondary dermatosis, but I feel that the evidence is such as to warrant its tentative acceptance for the present.

DR. C. GUY LANE, Boston: These 2 cases are minor editions of a case which Drs. E. M. Rockwood and A. M. Greenwood, of Boston, described some years ago (ARCH. DERMAT. & SYPH. **29**:574 [April] 1934). A patient came into the office with involvement of each groin, each axilla, the breast, ankles and mouth. If one can imagine the areas shown here today very much extended, sharply outlined, even more superficial and gradually extending, with the mouth perhaps three or four times as bad as in these cases, one can get a picture of that case.

At all times it was possible to obtain a pure culture of Monilia from the mouth. A bit of exudate being teased off, Monilia could be demonstrated to students at any time, and a pure culture could be obtained. The patient had much treatment, external and internal, with injections of various dyes and so forth, and not a thing ever made any inroad on the disease. It gradually progressed on his body, and he finally died in a hospital. At postmortem examination the pathologist was unable to determine the cause of death from gross study, but sections showed involvement of pulmonary tissue with definite mycelial threads, undoubtedly the same organism.

DR. JOHN GODWIN DOWNING, Boston: The finding of M. albicans on the skin is always of importance. In a series of 100 patients with normal skin on whom scrapings of skin were made, not one positive culture of M. albicans was obtained (Downing, J. G.; Nye, R. N., and Cousins, S. M.: Investigation of the Fungous Flora of Apparently Normal Skins, ARCH. DERMAT. & SYPH. **35**:1087 [June] 1937). This confirmed the work done by R. W. Benham and A. McH. Hopkins, who also failed to find M. albicans on normal skin. Where this organism is found one should always look for some constitutional disturbance. In 1 case of severe infestation of the skin by M. albicans the patient later died of tuberculosis (Downing, J. G., and Hazard, J. B.: Cutaneous Moniliasis Associated with Oral Thrush, ARCH. DERMAT. & SYPH. **31**:636 [May] 1935).

DR. MORRIS MOORE, St. Louis: This case is extremely interesting to me, principally because I was able to isolate on numerous attempts the organism ordinarily termed M. albicans, or as Dodge prefers, Syringospora albicans. Generalized moniliasis is not as rare as it is believed to be. As a matter of fact, I have observed a number of cases of extremely generalized involvement—in fact, more so than in the 2 boys presented here. In South America the disease is common, and I have observed a number of cases there, with de Almeida and in Rio de Janeiro, Brazil, with da Fonseca. The organism isolated in these cases is pathogenic. I tried it out on animals, and certainly it works wonders with them. It almost kills them, which is extremely unusual for organisms of this type. I can definitely state that this condition is moniliasis. In the groin, in the mouth and on the cheek it presents characteristics of a definite dyshidrosiform moniliasis.

A Case for Diagnosis (Folliculitis Ulerythematosa Reticulata?). Presented from the Barnard Free Skin and Cancer Hospital.

E. H., a white woman aged 44, entered the clinic in April 1938, with a pigmented dermatosis of the cheeks of thirteen years' duration. The onset of the condition immediately followed general anesthesia for perineal repair in 1925. At first the cheeks merely burned; later they became brown, scaly and pitted. There has been no change in thirteen years. There are no subjective symptoms. The past and family history are essentially normal. On examination, the skin over the lateral aspects of both cheeks presents a diffuse brownish pigmentation, interspersed with depigmented patches. The skin appears thickened but does not feel so. The individual lesions are small papules and pits, reticulated to produce a "pock-marked" appearance. There are no telangiectases. These areas are sharply

demarcated on the neck. Here a patch of smooth depigmented skin extends to both sides under the chin. In the right infraorbital region is an area about 1 cm. in diameter, with central erythema, some scaling, telangiectasia and atrophy. General physical and laboratory examinations gave essentially negative results. Histologic study showed slight atrophy of the epidermis, moderate flattening of the rete pegs and small areas of hydropic degeneration irregularly distributed throughout the corium. About the hair follicles there was a rather diffuse infiltrate of large lymphocytes, with an occasional giant cell of the Langhans type. The hair follicles were plugged with keratin. The sebaceous and sweat glands were normal.

DISCUSSION

DR. H. J. PARKHURST, Toledo: It is easier to tell what this condition is not than what it is. In spite of the reticular atrophy and the keratotic follicular plugging it does not appear to be folliculitis ulerythematosa reticulata as described by MacKee and Parounagian and by others. In that condition the patches appear gradually and almost imperceptibly during childhood. This woman states that her eruption appeared rather suddenly, following the administration of an anesthetic at the age of 31. The rather sharply outlined patch below the right eye is suggestive of lupus erythematosus, and it seems possible that the entire condition may be a degenerative process following lupus erythematosus. The histologic picture might bear this out. Certainly there are no epidermal horn cysts or tortuous follicles such as have been observed in folliculitis ulerythematosa reticulata, and the sebaceous glands were plentiful in the section.

DR. E. WILLIAM ABRAMOWITZ, New York: I am inclined to the view of the previous speakers that this condition is not classic folliculitis ulerythematosa reticulata, because of the absence of certain characteristic features of that disease. I should disregard the anesthetic that she was given many years ago as a cause. The condition may be grouped with the Riehl-Hoffmann melanosis that follows the use of impure or substitute products of petrolatum found in some cosmetics.

DR. LAWRENCE C. GOLDBERG, Cincinnati: This dermatosis was formerly confused with *acne vermoulante* of Thieberge and Brocq and was originally described by Pernet as symmetric facial atrophy and later as folliculitis ulerythematosa reticulata by MacKee and Parounagian. About 1923 Pautrier added the word erythema to the diagnosis in several cases which he had observed. Oppenheim gave this dermatosis another title, atrophoderma vermiculatum.

This patient presents comedos and a fatty type of cystic degeneration of the skin, which one does not see in atrophoderma vermiculatum; besides, the lesions of that condition are usually depressed, while these are elevated above the skin. I should like to suggest the diagnosis of an eruption caused by some chronically irritating petrolatum preparations, such as would be found in poorly and cheaply manufactured facial creams.

A Case for Diagnosis (Lichen Planus Hypertrophicus?). Presented by DR. CLINTON W. LANE and DR. JAMES W. BAGBY, St. Louis.

J. W. H., a white man aged 67, has had a lesion on the lateral surface of the left leg for several years. This has remained about the same size and has given no subjective symptoms.

On the lateral surface of the lower third of the left leg there is a tumor roughly the shape of an ear. Though well raised above the surface, it does not seem deeply to involve the underlying skin. It measures 2.4 by 3.2 cm. and is flat topped, with a central depression in the medial half. In the center of the patch is a thin yellowish dry adherent crust. The color varies from brownish red on the medial half to faint purplish on the outer half. It is firm to the touch, but is not tender.

The most striking pathologic change was seen in the central portion of the slide. The epidermis was moderately thickened; the pegs were hyperplastic. The rete cones were normal. In the upper part of the corium was an infiltrate which

appeared somewhat localized under higher magnification. This infiltrate was made up of lymphocytes and a few endothelial leukocytes.

Over several months the lesion was treated with a total of 350 international roentgen units of radiation filtered with 1 mm. of aluminum. This resulted in some flattening of the lesion and a slight fading of its color.

Hypertrophic Lichen Planus. Presented from the Barnard Free Skin and Cancer Hospital.

F. G., a white man aged 50, two years ago noted a small lump on the front of each leg. A year ago new lesions appeared on the legs and ankles and one on the right wrist. All have increased in size and now itch.

There are several sharply demarcated, irregular soft and rough elevated erythematous lesions with a pinkish elevated border on the anterior aspect of each leg. The surface is covered with adherent scales, under which in the central portions is a purplish tint. The lesions range from 0.5 to 4 cm. in diameter.

Microscopic study showed marked acanthosis and in the upper layers of the corium a broad band of infiltrate, consisting chiefly of lymphocytes, the lower limits of which were well demarcated.

Bullous Lichen Planus. Presented from the Barnard Free Skin and Cancer Hospital.

E. B., a white woman aged 61, states that six months ago vesicles developed on the hands. Within six weeks a crusted and eczematous eruption spread over the entire body. The condition has been progressive and accompanied with severe itching.

The forearms and the entire lower two thirds of the body are involved, the palms and soles being free. The skin presents a mottled eruption of erythematous plaques and macules and some crusting and vesiculation. Excoriations are present and many tiny fissures with exudation of serum.

Histologic study showed vesicles and vesicopustules, some extending into the corium.

On Sept. 21, 1938, she was given routine treatment for contact dermatitis. One week later firm erythematous indurated spots suggestive of erythema multiforme appeared on the upper part of the trunk and shoulders. In another week many flat shiny papules (lichen planus papules clinically) covered the extremities and back, with a few small bullae on the oral mucosa. A few vesicles and bullae appeared on the extremities, being most marked about the ankles. About two weeks later she was put on small doses of phenobarbital.

NOTE.—This condition cleared temporarily under mercurial injections but later recurred as typical chronic pemphigus vulgaris.

DISCUSSION ON CASES OF LICHEN PLANUS

DR. CLARK W. FINNERUD, Chicago: In the first case I first thought the clinical appearance of the lesions was strongly suggestive of Bowen's disease or a type of malignant dyskeratosis closely related histologically. There is no such suggestion in the sections, and I cannot classify the picture definitely with hypertrophic lichen planus, but because one portion of the section is mildly compatible with hypertrophic lichen planus, it seems most probable that the condition is an extremely atypical example clinically of that disease. I think the section may have been taken from an unfortunate part of the lesion. Possibly because of the roentgen therapy that has been employed the previous histologic changes have been destroyed. If another section is taken a few months hence, it is possible the diagnosis can be settled.

I believe that the second case clinically and histologically may properly be considered one of hypertrophic lichen planus. There are some unusual features about it, particularly, as in the first case, the facts that the lesions are soft and

that possibly as a result of treatment the margins are rather acutely inflammatory, a change not characteristic of that disease. I should be inclined to accept the case as a proper instance of hypertrophic lichen planus.

As to the third case, in the few cases of bullous and erythematous lichen planus that I have had the opportunity to observe, there have been, almost without exception, few characteristic papules of lichen planus. This elderly woman did have some flat papules on the backs of the hands, particularly the left, which were pretty fair lichen planus papules. On the flexor surface of the left, where lesions had involuted, there were more or less characteristic shape and sepia coloration. I think the diagnosis of bullous lichen planus in this case is probably correct.

Dr. Richard S. Weiss, St. Louis: The woman came under observation at the Barnard Free Skin and Cancer Hospital a few weeks ago with an eruption that was not nearly as widespread as the present eruption. It consisted of lichenoid papules, some of which were typical of lichen planus, on the trunk, particularly on the scapular areas, the arms and the sides of the thighs. The individual papules were definitely elevated, plane-topped and angular; the color was almost consistent with the usually described color of lichen planus, and there were a small number of vesicles, scattered chiefly about the ankles, with some on the arms, and three or four bullae in the mouth. That was the picture when my associates and I first saw the patient.

She came into the hospital a week or so later, and the eruption began to be more progressive. The vesicles about the ankles looked like a chemical dermatitis. They did not seem to be connected with any individual papules. At that time we thought she had vesicular or bullous lichen planus; she was hospitalized and given phenobarbital. She got sick a few days after that, with fever and malaise, and she was sick this morning when presented, although her temperature has gone down. Now it is possible that some of the bullous eruption is a bullous erythema due to phenobarbital. However, I must say this, that she had bullae in the mouth, and she had this vesicular eruption about the ankles and in other areas before she was given any of the barbital group of drugs, at least to our knowledge.

The members will recall that Engman Sr. some twenty-five years ago described a vesicular type of lichen planus, and we felt sure when we first saw this patient that we had another case of that type to deal with. There is a remote possibility, it seems to me, that we are dealing with a case of pemphigus beginning in a most peculiar manner.

Dr. Joseph Grindon, St. Louis: I did not have the advantage Dr. Weiss had of seeing the patient at the beginning, when, he says, there were angular papules similar to those of lichen planus. However, I have looked over the patient and could not find a single lesion that I should call lichen planus. The condition, according to her statement, has existed since May and has come out in a series of crops. She said lesions had been continuously present, but a number of new lesions would come out with a rush. Then there would be amelioration, followed by another rush. That taken with the itching, the rough symmetry, the distinct grouping in places and the character and size of some of the bullae—for example, on the left arm—all seem to me to justify a diagnosis of dermatitis herpetiformis.

Dr. Andrews alluded to the fact that there were other lesions. I do not believe he thought, and I surely did not think, that the bullous lesions were due to a drug, but there are on the flanks and at other points fine macules which do not fit in with a diagnosis of dermatitis herpetiformis. I believe they are due to the phenobarbital which she has been taking.

Chronic Atrophic Lichenoid Dermatitis. Presented from the Barnard Free Skin and Cancer Hospital.

L. B., a white man aged 60, first noted a small white spot on his right shoulder twenty-five years ago. This has enlarged slowly. About fifteen years ago other similar lesions began to appear on his chest and abdomen. No new lesions have

appeared in the past three years, nor have the old ones enlarged. There are no symptoms. He had leukoplakia of the penis, which developed into squamous cell carcinoma, and the penis was amputated in 1937, at which time the condition of his skin came under attention. On the chest, back and abdomen are seen a number of lesions varying from 1 to 8 cm. in diameter. They are atrophic and irregular in shape, the older lesions being depressed. They are sharply circumscribed, white and covered with a fine white scale. A histologic section showed a thinned epidermis with absence of rete pegs. The vessels in the corium were few. There was a little infiltrate and condensation of collagen bundles in the lower part of the corium. Weigert's stain demonstrated a decided decrease in elastic tissue. There has been no change in the patient's condition in the year he has been observed.

DISCUSSION

Dr. Oliver S. Ormsby, Chicago: This case, presented under the title "chronic atrophic lichenoid dermatitis," recalls the controversy that took place years ago in the discussion of the early cases, described under the title "white spot disease." In order to clarify my present discussion I shall briefly review the debatable reports. Westburg (*Monatsh. f. prakt. Dermat.* **33**:355, 1901) described a patient with atrophic white lesions on the chest and shoulders under the title "white spot disease." Shortly afterward J. C. Johnston and S. Sherwell, of New York (*J. Cutan. Dis.* **21**:302, 1903), described a second case. During this time I had had 2 patients presenting similar symptoms under observation in Chicago. In 1907 the late Dr. F. H. Montgomery and I (*J. Cutan. Dis.* **25**:1, 1907) described these 2 together with a case of typical lichen planus sclerosus et atrophicus (Hallopeau). A clinical and histologic study was recorded, and 8 previously reported cases were discussed. This review showed that all the patients had been women and that the lesions had been practically limited to or chiefly located on the neck, shoulders and upper portion of the chest and back. The individual lesions were characterized by the sharp outline, peculiar whiteness, small size, tendency to remain discrete even when grouped into patches and absence of distinct elevation. Our conclusions were that the cases of so-called white spot disease recorded up to that date were examples of either morphoea guttata or lichen planus sclerosus et atrophicus. In 1910 I presented a paper before the Section on Dermatology of the American Medical Association on lichen planus sclerosus et atrophicus (*J. A. M. A.* **55**:901 [Sept. 10] 1910), reporting a clinical and histologic study of 6 cases—5 new ones—and again reviewing the literature, with the same conclusions. J. Csillag's case recorded in 1909 (in Neisser, A., and Jacobi, E.: Ikonographia dermatologica, Berlin, Urban & Schwarzenberg, 1909, no. 4, p. 147) was placed provisionally by me in the group of lichen planus sclerosus et atrophicus. In 1914 another case of white spot disease was described in this country by G. M. MacKee and F. Wise (*J. Cutan. Dis.* **32**:629, 1914). In their case the lesions were situated on the lower part of the trunk; they were white atrophic spots resembling those in other recorded cases, and after a discussion of the case together with the literature, the authors came to the same conclusions that Dr. Motgomery and I had arrived at eight years previously, namely, that all these cases of so-called white spot disease belong in one of two groups, with cases of scleroderma or of lichen planus. In 1928 Dr. Wise and Dr. Bedford Shelmire described a case of Csillag's disease in Dallas, Texas (Arch. Dermat. & Syph. **18**:179 [Aug.] 1928). I also saw the patient. There were white oval rounded or irregular well defined papules, some surrounded by a pink areola or a narrow zone of pigmentation. By coalition of papules, plaques of varying dimensions were formed, in which the identity of the papules remained. The patches like the individual papules were oval, rounded or irregular and usually had a pigmented border. There were no horny spines and no depressions from which such spines might have fallen. Histologically the corium showed collagenous degeneration, and the elastin showed structural changes up to complete obliteration in places. The authors concluded from this study that the condition was distinct from both the lichen planus and the scleroderma group and should be considered a separate entity.

Previously Dr. Wise had placed Csillag's original case in the lichen planus group. Csillag's original description was different from that just outlined. He described pale red mixed with chalky white small areas and larger plaques, on the surface of which were horny plugs connected with pilosebaceous openings. It is interesting to note that he considered the condition identical with von Zumbusch's lichen albus, which is a member of the lichen planus group.

It may be said that there are three distinct diseases characterized by peculiar white lesions: localized scleroderma (morphoea guttata), lichen planus sclerosus et atrophicus and lichen planus with atrophy.

Practically all the recorded cases of white spot disease were instances of localized scleroderma (morphoea guttata), characterized by nonelevated peculiar white soft lesions of variable size, situated largely on the upper part of the chest and back, usually in women. Lichen planus sclerosus et atrophicus is characterized by white distinctly elevated oval, rounded or irregularly shaped papules, each of which usually presents on its surface two or three or more black horny plugs or small depressions from which these plugs have fallen. Plaques and patches are frequently formed by the grouping and evolution of these papules. The patches and plaques are usually situated on the clavicles or on the upper part of the back, over the shoulders. They are seldom generalized, and in them the papules, including the black horny plugs, retain their identity. In rare instances the brownish red irregular flat-topped lichen planus papule undergoes atrophy, leaving white atrophic scars. The disease is readily distinguished from the two previously described by the presence of numerous lesions of ordinary lichen planus. Subjective symptoms are present in the last-named disease but absent in the other two.

In the case before the organization the characteristics are those of lichen planus sclerosus et atrophicus rather than of Csillag's disease. The early lesion is a white papule, and while there are no black plugs, there are pilosebaceous openings from which the horny spines have probably been exfoliated. The histologic picture is also compatible with this diagnosis.

Leukaemia Cutis. Presented from the Barnard Free Skin and Cancer Hospital.

J. L., a white man aged 54, entered the clinic in May 1936, with a nodular eruption on the face and forehead of three years' duration. The condition began as a small "pimple" on the left cheek, which was soon followed by the appearance of similar lesions on the face. They increased in size and itched considerably.

The patient was born in Russia of Jewish parents. The family and personal history are otherwise insignificant.

The general physical examination gave essentially negative results.

Examination of the skin shows several discrete soft nodules on both cheeks and the forehead. They are pinkish red, vary in size from that of a split pea to that of a hazelnut and are not tender or fixed to the subcutaneous tissue. Similar lesions on the right side of the neck and each deltoid region are seen. All the superficial lymph nodes reveal many small firm discrete nonmatted painless nodes.

The white blood cell count varied from 6,500 to 11,500, with a typical differential count, of 20 per cent neutrophils, 3 per cent eosinophils, 2 per cent basophils, 9 per cent monocytes and 65 per cent lymphocytes, with no immature forms. A roentgenogram of the chest was essentially normal. The tuberculin and the Kahn test were negative.

Histologic examination showed normal epithelium. Within the corium a localized area of circumscribed infiltrate consisting of lymphocytes was seen. A scant stroma and vascularity were present.

Chronic Lymphatic Leukemia, Possibly Accompanied with Leukaemia Cutis and Late Syphilis of the Skin. Presented by the Clinics of Washington University School of Medicine.

I. F., a Negress aged 55, has had generalized enlargement of lymph nodes, weakness, loss of weight and an eruption on the face, all occurring in the past eighteen months. She acquired syphilis from her first husband at the age of 16,

and antisyphilitic treatment was begun sixteen years ago. She chews tobacco and drinks beer occasionally, but uses no drugs. Her appetite is good, and she sleeps well.

The cervical glands are enlarged. The lungs and heart are essentially normal. The abdomen is slightly enlarged, but the spleen is not palpable. There are enlarged epitrochlear, axillary, inguinal and femoral lymph glands, which are discrete but not tender. The blood pressure is 165 systolic and 90 diastolic. Examination of the blood showed 660,000 white cells, 3,590,000 red cells and a differential count of 1 per cent segmented cells and 99 per cent lymphocytes.

Histologic examination showed ulceration and atrophy of the epidermis. Throughout the corium and subcutaneous tissue were aggregates of infiltrate. These areas were made up of lymphocytes and giant cells of the Langhans type with a moderate amount of necrosis scattered throughout the infiltrated areas.

On July 7, 1938, she was given solution of potassium arsenite, 5 drops three times daily. On July 18 the white blood cell count had dropped to 290,000, and the dose was increased to 10 drops three times daily. On August 15 she complained of diarrhea with increased pain and swelling in the cervical glands. The arsenical was discontinued, and she was referred for roentgen therapy. An August 25 an eruption appeared on the face, neck, chest, arms and legs. On August 29 there was a lichenoid papular eruption on the left side of the neck. Some of the lesions were rather soft tumor-like masses with a rather reddish color. On the arms, chest and legs there was an acuminate papular eruption, which was widespread and pruritic. The diagnosis at this time was arsenical dermatitis on the chest, arms and legs and leukaemia cutis on the face. A soothing lotion was prescribed, and in about one week the chest, arms and legs had entirely cleared. The lesions on the face remained and are still present. She has had about eleven roentgen treatments, and the lymph glands, while still noticeable, have decreased in size. The white blood cell count remains around 300,000.

DISCUSSION OF CASES OF LEUKEMIA

DR. H. N. COLE, Cleveland: The man's lesion clinically has somewhat the appearance of sarcoid. One might also think of leprosy. It is possible only by the histologic examination and study of the blood to arrive at a conclusion in regard to this particular condition. The fact that 65 per cent of the white blood cells are of the lymphocyte type would speak more in favor of lymphoblastoma developing from the myeloblast as the stem cell. Nevertheless, there were 9 per cent monocytes, and the possibility must be kept in mind that a monocytic type of disease may develop later or that the lesions may become a chronic type of lymphatic leukemia.

The woman's cutaneous lesions certainly are not characteristic. I shall grant that she has chronic lymphatic leukemia. The specimen of tissue would speak in favor of granuloma. I am undecided whether to call it syphilis or tuberculosis. The patient has some small ulcerative lesions on the cheek, and she also has a group of nodules on the lobule of the ear, which might well go with a tuberculous type of process.

DR. HARRY M. HEDGE, Chicago: This man has had the primary lesion for three years, and the secondary lesions developed over a period of several months. His peak condition was not of the best. There was no ulceration of the nodules, although he had several nodules over the face and arms and some on the legs. The Kahn and the tuberculin tests were negative. He was in excellent general health during the entire attack.

This calls to mind the case I presented before the Chicago Dermatological Society on Oct. 20, 1937 (ARCH. DERMAT. & SYPH. **37**:698 [April] 1938). The man came into my service at the Evanston Hospital, complaining first of an ulcer on the right little finger, with nodules ascending the lymphatic vessels of the arm, resembling closely tularemia. He was a PWA worker, working in grasses out in woods that might have been frequented by wild rabbits. Examination of the

blood was made, and an agglutination test for the bacillus gave negative results. A blood count showed 97,000 white cells, 91 per cent of which were lymphocytes. This man had been entirely well until this acute attack, when headaches, malaise, loss of appetite and a general downward trend in health occurred. He became weaker and died in about six months—of septicemia, not of the lymphatic leukemia.

At autopsy it was possible to complete the diagnosis of semiacute lymphatic leukemia, and in histologic sections made the typical lymphatic tissue filled with lymphocytes was seen. The patient had lesions on the arms, the legs, the trunk, the scalp and the buttocks, and a great many of these lesions had ulcerated. The interesting part of this particular case was the fact that the disease came on so acutely with no premonitory symptoms, and that the complete course leading to death covered six months.

Danlos' Syndrome, Associated with Congenital Lipomatosis. Presented by Dr. Norman Tobias, St. Louis (from the Firmin Desloge Hospital).

M. G., a white girl aged 14 years, was seen first at the Firmin Desloge Hospital in 1936. The mother stated that up to the age of 2 years the patient had attacks of cyanosis; the extremities chiefly were involved. It was also noted that the child's skin was extremely fragile and easily split, leaving disfiguring scars. At the age of 2 years "knots" in the deep subcutaneous tissue over the calves, arms and buttocks were discovered. No history of hereditary involvement could be discovered. The parent and 3 siblings were normal in every respect.

General physical examination revealed a slight brunette. The hair was silky to the touch. The nails presented longitudinal striations. The teeth were regular. In all other respects she was normal.

On examination the skin has a peculiar velvety texture. The bony prominences are readily felt because of a decrease in subcutaneous fat. A few dilated capillaries are present on the cheeks. On the anterior portion of the trunk small venules are visible. Numerous scars are present. At no time have bullae followed trauma, but a "splitting of the skin" occurs, followed by "bruises." Over the prominences of the elbow joints and knees are numerous soft depressed violaceous atrophic scars resembling waffle markings. The skin over the tibias and ankles is also covered with depressed pinkish cicatrices. The joints of the thumbs, fingers and wrists can easily be hyperextended. The index finger can be hyperextended to touch the dorsal surface of the hand. Direct traction on the metacarpophalangeal joints stretches the capsule and permits an extension of 3 cm. The hyperlaxity is most evident in the joints of the thumbs. Hard smooth shotlike subcutaneous tumors can be felt anteriorly over the fibulas and posteriorly on the arms, forearms, buttocks and calves. They are not attached to the skin and are fully movable in the subcutaneous tissues. The hyperelasticity of the skin, which is general and bilateral, is more pronounced in the skin of the cheeks, thighs and legs when stretched. The tabulation shows the difference in elasticity between the skin of the patient and that of a normal child:

	Patient	Normal Child
Cheek	2.5 cm.	1.7 cm.
Chin	1.5	1.2
Arm	3.0	1.6
Forearm	4.2	1.5
Thigh	4.6	1.5
Leg	4.6	1.0
Neck	2.5	1.5

Laboratory examinations showed 3,000,000 erythrocytes, 58 per cent hemoglobin (Dare) and 7,900 leukocytes, with a differential count of 4 per cent stab forms.

43 per cent segmented neutrophils, 50 per cent lymphocytes, 1 per cent monocytes, 1 per cent eosinophils and 1 per cent basophils. The serum calcium content was 6.4 mg. per hundred cubic centimeters. The basal metabolic rate was + 15 per cent. All other laboratory examinations, including roentgenograms of the long bones, skull and chest, revealed no departures from normal.

Histologic examination (fig. 3) showed the skin to be unusually thin. The epithelium was apparently normal. The corium contained three or four times the normal number of elastic fibers, which seemed to be more delicate and more compact but less dense than normal. In place of the usual loosely woven but thick bundles of collagen fibers there was a fine-meshed well separated fibrillar structure.

Fig. 3.—Danlos' syndrome, showing a great increase in the number and size of elastic tissue fibers.

The fibrils seemed to maintain their identity rather than to form bundles. The elastic fibers mixed diffusely with the collagen fibrils. There was a superabundance of sweat glands coiled in masses two or three times the size usually found. There was no cellular reaction about any of the integumental structures. The vessels appeared to have unusually large lumens and thin almost insufficient-looking walls. Examination of the lipomas showed well defined fibrous capsules about each round or oval fat lobule. The capsules contained mostly collagen fibers, but also a few scattered elastic fibers. The fat cells within the lobules were normal for the most part, although some were filled with a material looking more like mucus than true fat. There was no wandering cell reaction. The vessels

appeared to be more abundant than one would expect in the interstitial capsules of the lobules.

The patient has been under observation for two years, during which time no new lipomas have developed, and some appear to have become smaller.

NOTE.—F. P. Weber and J. K. Aitken (*Lancet* **1**:198 [Jan. 22] 1938) have explained the formation of the lesions previously described as lipomas as follows:

"It seems that the presence of freely movable subcutaneous spherules, in considerable numbers, especially in regions where the skin is loose (cutis laxa), may be included as a fifth main sign of the Ehlers-Danlos syndrome, though it has not been recorded in most cases. Further observations are necessary to show in what proportion of cases this sign is present. The spherules are apparently not true lipomata, but result from a deviation in the normal type of fat growth—namely, from the arborescent (bud-like) development of small lobules from the subcutaneous fat. These lobules, after almost losing their pedicles and blood-supply and with thickening of their capsules, constitute hard spherules freely movable in the subcutaneous tissue. Probably in time they become minute oil-containing cysts, with thickened fibrous or even calcareous walls."

DISCUSSION

DR. NORMAN TOBIAS, St. Louis: Since I described the first case of Danlos' syndrome in the American literature, I have attempted further investigation of this condition. I think it is evident to all dermatologists that this disease is more than a dermatologic curiosity. There is a possibility that a disturbance of the visceral elastic tissue is associated with the cutaneous features. If these cases could be followed for evidence of aortic dilatation, megacolon and disturbance of the hollow viscera, a great deal more could be learned about the Danlos syndrome. Since I described this case in 1932, many other cases have appeared in the literature. At the present time 32 cases have been described in the world literature.

About two years ago I took a biopsy specimen of the stretched skin of this patient to determine the nature of the damage to the elastic tissue; I observed that not only the elastic tissue but the collagen bundles were damaged. I think that is the answer to the peculiar scarring that occurs in such cases, which I think all the members noticed on the knees and elbows of this girl.

Danlos' Syndrome. Presented from the Clinics of Washington University School of Medicine.

O. O. Y., a white youth aged 17, was first seen at Barnes Hospital on Oct. 27, 1937. Since he was 7 months old the skin has been observed to "break easily." On breaking it bled a little, but oozed a yellow fluid. Such breaks healed in two to three weeks and were frequently infected. The general health has been good with the exception of frontal and parietal headaches about twice weekly. General physical examination reveals a well developed boy 5 feet 11 inches (180 cm.) tall and weighing 156 pounds (70.8 Kg.). There are scattered local areas of hypesthesia; otherwise the findings are normal. The laboratory findings were normal except for the presence of 8 per cent eosinophils.

On examination the skin is extremely "loose" and in many places can be picked up and stretched 4 to 8 cm. away from the underlying tissues. The scalp is rather rugose and presents the same elastic features. On the extremities numerous thin scars are found, with some on the body, and some of these scars "balloon" outward, giving the appearance of pseudotumors. The latter are especially noticeable on the left elbow and wrist and on the extensor surfaces of the legs and knees.

Examination of the joints reveals that many of them can be hyperflexed to a marked degree. This patient presents the four criteria for the diagnosis of the Danlos syndrome: (1) hyperelasticity of the skin; (2) hyperlaxity of the joints; (3) fragility of the skin, and (4) pseudotumors following trauma.

Histologic examination showed the epithelium to be somewhat thin and wavy in places. The collagen fibers in the subepithelial layers did not have the usual orderly arrangement, and the fibers appeared to be short, as if they had been fragmented. Instead of lying in parallel strands, they coursed in all directions and made various angles with each other. There was a striking increase in the elastic tissue fibers and in the white fibrous connective tissue, with lengthening and thickening of the bundles.

A Case for Diagnosis (Morphea?). Presented by DR. CLINTON W. LANE and DR. JAMES W. BAGBY, St. Louis.

M. P., a white woman aged 67, burned her thigh three years ago with an overturned pot of hot tea. The burned area has remained red, and recently new

Fig. 4.—*A*, Danlos' syndrome; *B*, pseudotumor following trauma.

areas have appeared elsewhere on the body. These have all appeared within the last few months. There have been no subjective symptoms. She has been taking "u-reduce" capsules for the past few months, but no other internal medicine. (U-reduce, according to the advertising, is composed of celery, cranberries, sea tang, Irish moss, rhubarb and spinach in gelatin capsules and contains no other ingredient; the preparation has not been examined in the laboratory of the American Medical Association.) She has had arthritis in various joints for a number of years and a mucous colitis, which is controlled by dietary measures.

Nummular and larger purplish red disks are present on the abdomen, back and hips. These are slightly raised and somewhat firm to the touch and fade on pressure. They are not tender and vary from 2 or 3 to 10 or 12 cm. in diameter. The largest is present in the right inguinal region. In the central portion of many patches there is a pearly sheen. The newer patches appear as dull red macules

and vary in size from that of a pea to that of a button. In a few the central portion is white, and in others there is a pearly sheen.

Histologic examination of a lesion from the back showed the epidermis to be normal. Throughout the corium there were an infiltrate and edema. The infiltrate was patchy and under higher magnification was seen to be made up of lymphocytes and an occasional fibroblast and endothelial leukocyte.

Scleroderma. Presented by DR. JOSEPH GRINDON and DR. JOSEPH GRINDON JR., St. Louis.

R. W. L., a white man aged 68, presents a condition which began twenty-three years ago. During the past eighteen years there has been little extension. There is complete involvement of the face, scalp, neck, forearms and backs of the hands and some ectropion. Two wide partially atrophic bands, bordered by a narrow pink zone of dilated venules, extend down the front of the chest. The width of the bordering erythematous zone has varied from 3 to 6 inches (7.6 to 15 cm.) or more within a few days.

DISCUSSION

DR. PAUL A. O'LEARY, Rochester, Minn.: I agree with the diagnosis of morphea in the case of Drs. Lane and Bagby, and I believe that leprosy and drug eruption can be readily eliminated from the diagnostic possibilities.

In the case presented by the Drs. Grindon there is another manifestation of localized scleroderma, the terminal or end stage of the disease, evidenced by the atrophy on the back of the neck and calcareous deposits pretty well scattered throughout the skin of the face. A point about morphea worthy of general comment is that it frequently involutes, although occasionally a little thyroid medication or application of heat and massage may hasten its involution and the appearance of the characteristic atrophy. As this stage is the end result of the sclerodermatous process and the calcium has been present so long, I have no suggestions to offer for treatment. One other point that I should like to make in regard to the atrophy of scleroderma is that I believe atrophy is a definite feature of scleroderma and not another entity. Hence, the use of the term idiopathic atrophy is not justified in this condition, as the atrophy that follows the involution of the cutaneous sclerosis is not idiopathic in the sense in which this word is ordinarily used.

Erythema Multiforme Bullosum. Presented from the Barnard Free Skin and Cancer Hospital.

W. B., a white woman aged 25, first noticed her eruption suddenly one year ago, with itching on her extremities. The patient says that vesicles appear only after scratching. It has been possible to watch her produce them in fixed areas after rubbing. The eruption is principally on the extremities and buttocks. She has had a few lesions over the body. The mucosa about the nares has been involved. Lesions heal in the center and spread peripherally, forming irregular patches that sometimes run together. Pigmentation results as they fade. Laboratory tests gave negative results. A histologic section showed vesicle formation in the lower part of the epidermis and sometimes in the corium and some infiltrate of lymphocytes and polymorphonuclear cells in the upper part of the corium. The patient has improved only slightly under administration of salicylates, arsenic and mercury in various forms by mouth. New vesicles continue to form if she traumatizes the skin.

Senear-Usher Pemphigus. Presented from the Barnard Free Skin and Cancer Hospital.

A. M., a white woman aged 68, was first seen in 1933, when she had noted blisters on her forehead and arms for three weeks. These would break, form crusts and slowly heal. She had had vitiligo on her arms for several years. The

lesions are limited to the face, arms and neck. The bases of the older lesions are erythematous, and some show atrophy resembling lupus erythematosus. The Pels test gave a phytotoxic index of 53. The Welsh test for pemphigus gave a positive result. Other laboratory studies were normal. A histologic section showed separation of the epidermis from the cutis by bulla formation. The epidermis was moderately acanthotic and in places atrophic. A moderate infiltrate of lymphocytes was seen in the upper part of the corium. During the past five years the patient has had considerable treatment, with little result. Administration of viosterol and calcium and injections of iron cacodylate, a gold preparation and moccasin venom have all been tried, with little effect.

DISCUSSION

DR. F. E. SENEAR, Chicago: With regard to the case presented as one of erythema bullosum, I feel that it is rather a case of dermatitis herpetiformis. The patient has had the disease for a year continuously without any remissions, and there is intense itching and intense pigmentation. The latter manifestation might result from a prolonged attack of bullous erythema, and it might be influenced in part by the ingestion of an arsenical. Furthermore, where the lesions are not of the large circinate variety, they are grouped and with their coalescing and inflammatory reactions produce a base on which the individual lesions now show. I should regard the condition as dermatitis herpetiformis, in spite of the fact that some of the lesions on the breast, the hands and the patellas show a more or less typical picture of herpes iris. There are lesions of that type in dermatitis herpetiformis.

With regard to the second case, I dislike on the basis of a single observation to dispute the ideas of those who have observed it for five years, but on the evidence presented today I do not feel that it can be accepted as a case of pemphigus erythematodes. To be sure, the patient has had lesions on the face and is said to have had lesions of the nasal mucosa and the palate. None of these are present today. There is no mention in the description of any picture on the face in the early stages suggesting either lupus erythematosus or seborrheic eczema of the congestive type, such as would be expected in the benign form of pemphigus. Moreover, neither the rather large patch on the right arm, a location not involved in the pemphigus type unless the eruption is extensive, nor the lesions on the upper part of the chest suggests any of the end results expected in that disease, viz., the greasy or dry keratotic lesions, usually more or less seborrheic. If I had to label this disease, I should call it, particularly from the appearance of the lesion on the right arm, a form of lupus erythematosus, although not typical in appearance, rather than a form of pemphigus combining certain features of lupus erythematosus.

A Case for Diagnosis (Nevus). Presented by Dr. G. V. STRYKER, St. Louis, and DR. H. C. GEHRAND, St. Louis (by invitation) (from the Dermatologic Service of the St. Louis City Hospital).

L. S., a white woman aged 22, mentally defective with psychotic episodes and an intelligence quotient of 54, has congenital malformation of the legs and three congenital hernias. There have been progressive enlargement of the left leg and developmental growths in the skin. Both parents are said to be mentally defective.

General physical examination reveals a small fairly firm globular mass just lateral to the left nipple, which appears to be attached to the underlying structure but not to the skin. Pressure on this mass produces serosanguineous fluid from a small opening 0.5 cm. from the nipple. There is a vascular nevus about the size of a large grapefruit on the abdomen. An irregular tumor mass is felt just below the umbilicus.

On examination of the skin, the left plantar surface and toes are seen to be involved in a massive overgrowth of the connective tissue elements of the corium. In some areas the epithelium has responded with a verrucous type of hypertrophy.

This same process is going on to a limited extent on the right foot. Naevus unius lateris is distributed over the left side of the trunk, axilla, arm and hand. There are multiple large nevi scattered irregularly over the body.

Roentgen examination of the skeletal system showed the following interesting phenomena: The intervertebral spaces in the cervical portion of the spine were obliterated, with partial fusion and impaired function. The diameter of the shaft of the left humerus was increased in the upper third; the bones of the right wrist showed a developmental deformity, and the ulna was shortened. The radius showed bowing, associated with Madelung's deformity. There was curvature of the lumbar vertebrae to the left, with a compensatory tilting of the pelvis to the right. There was marked bowing of both tibias and the left fibula and tarsal, and metatarsal bones were fused and the ankle joint almost completely obliterated; the bones of the right leg were also deformed to a lesser degree. There was enlargement of the proximal phalanx of the left index finger, with obliteration of the joint at the first interphalangeal articular margin; the phalanx of the left middle finger was also enlarged, and there was enlargement of the proximal and middle phalanges of the right index finger.

Ichthyosis Hystrix (Naevus Unius Lateris). Presented from the Barnard Free Skin and Cancer Hospital.

E. S., a white woman aged 18, has an eruption which began on the hands at the age of 2 weeks and slowly spread over the entire body. At the present time there are linear verrucous lesions with areas of apparently normal skin between. The right half of the body is affected about twice as much as the left. The lesions are linear and run parallel to the course of the blood vessels and nerves. In the folds of the body there is more hyperkeratosis than elsewhere. The family history was irrelevant.

A histologic section showed intense hyperkeratosis. The epithelium was atrophic in areas and showed moderate edema. There was some dyskeratosis. She has improved little under treatment. Fever therapy caused some remission, but the original condition promptly returned. The destruction caused keloid formation.

DISCUSSION OF CASES OF NEVUS

DR. G. V. STRYKER, St. Louis: Our case represents a congenital defect which probably had its origin in the germ plasm. There are signs both of the Bourneville-Pringle syndrome, also known as tuberous sclerosis, and of Recklinghausen's neurofibromatosis. In all probability these two diseases overlap and are interrelated and the picture in this case is simply a bizarre one which has the characteristics of both diseases.

Generalized Xanthomatosis. Presented from the Barnard Free Skin and Cancer Hospital.

B. H., a white woman aged 55, first noticed yellowish lesions on her hands eight years ago. These appeared later about the eyes, mouth, back, knees, elbows and feet. There was at times a burning sensation in the nodules. There was no family history of diabetes. Shortly after admission a diagnosis of cholecystitis was made, and the gallbladder was removed in 1934. A small scarred liver was found. After this the cutaneous lesions practically disappeared for several months. They have slowly reappeared. The typical yellow to orange tumors are seen in some areas in linear formation. They are from 2 to 10 mm. in diameter. Blood cholesterol determinations have shown from 340 to 590 mg. per hundred cubic centimeters. The total blood lipoid content was 114 mg. per hundred cubic centimeters. Other laboratory studies gave negative results. Histologic sections confirmed the diagnosis.

DISCUSSION

DR. E. W. NETHERTON, Cleveland: This case is one of the startling examples of a systemic condition with cutaneous manifestations. The disease is complex; it is based on a disturbed metabolism of the lipoid substances as well as storage of the lipids. The solution rests with the chemist. I feel that all patients with this disease should be thoroughly studied from the standpoint of the chemistry of the fats, fractions of the various lipoid substances in the blood as well as tissue from the lesions, when obtainable, being studied. The patients should be studied carefully for various systemic disturbances which may contribute to the production of xanthomatosis. This is particularly emphasized by the excellent work of Hamilton Montgomery (*J. Invest. Dermat.* **1**:325 [Oct.] 1938), in which he has studied the possibility that damage to the liver was a factor in this particular syndrome.

Urticaria Pigmentosa. Presented by DR. NORMAN TOBIAS, St. Louis.

C. S. C., a white girl aged 1½ years, was born with an eruption over the entire body. This has gradually deepened in color, but there has been no itching. There have been no other cases in the family.

There is a generalized eruption of light and dark brown macules of various sizes scattered over the entire body. None of the lesions has shown wheals. The Wassermann and the Kahn test were negative, and blood smears showed no pathologic changes. The nonprotein nitrogen content of the blood was 33 mg., the sugar content 85 mg. and the cholesterol content 187 mg. per hundred cubic centimeters. A roentgenogram of the chest was normal.

Histologic examination showed moderate acanthosis with a slight infiltrate consisting of lymphocytes and mast cells in the upper part of the corium. A section stained with sudan III did not show fat. The patient has been treated with vitamin C, but no definite improvement has resulted.

DISCUSSION

DR. S. W. BECKER, Chicago: This patient has so-called juvenile urticaria pigmentosa, but when it is realized that this condition appears predominantly in the first year of life—50 per cent in the first six months—after which there is a gradual diminution till the age of 50—it is difficult to decide when a condition is of the juvenile type and when of the acquired type. The lesions started as redness and swelling, later followed by hyperpigmentation, probably postinflammatory. Occasionally the pigmentation appears first, but the preceding erythema may have been missed. This erythema persists for a few hours and then gradually fades out. There is a tendency to urtication on application of friction, heat, cold or various types of irritants, which disappears as the duration of the disease becomes longer. It is interesting in this case because these lesions no longer become urticarial on friction, and the mother states that the condition is improving.

The chief observation under the microscope typically is a basophilic mast cell infiltration about the vessels in the superficial part of the cutis. Occasionally these basophilic granules are lacking, and in one specimen sent in by M. J. Reuter I observed abundant cellular infiltrate with cells of the same type but with eosinophilic content. I showed this section to Prof. H. Pinkus, who visited the clinic; he stated he had never seen one like it, and it was not reported in J. Jadassohn's "Handbuch der Haut- und Geschlechtskrankheiten" or in O. Gans' "Histologie der Hautkrankheiten."

Urticaria pigmentosa is unique in dermatology for this intense basophilic infiltration, and the significance of basophilic cells is unknown. The pigment of the spots is melanin. There have been some experimental studies. Boymer rubbed with nettles for four days the arm of a 20 year old man with urticaria pigmentosa and then excised the section. He saw polymorphonuclear cells, adventitial cells and basophils. Blumer was unable to confirm this. In 1 case I tried injecting

histamine into the skin. A wheal was produced but not followed by hyperpigmentation. There are many different opinions about this condition. Török, who wrote about the condition in Jadassohn's handbook, stated that these lesions are nevi, with which I cannot agree. In the first place, the lesions appear at varying times, often preceded by the wheal. There are no nevus cells in these sections, although sometimes the basophilic cells appear somewhat like ordinary nevus cells. The *cellules claires* in the epidermis are never increased in number. The condition is evidently an inflammatory lesion of unknown cause, usually characterized by a large number of basophilic cells with overlying postinflammatory melanosis.

As regards treatment, Drs. Fox and Michael recommended roentgen irradiation, which I found to be of some benefit to a condition appearing in the thirties, in that after the administration of several roentgen treatments the lesions ceased to urticate when they were rubbed or when the patient took a hot bath.

Xeroderma Pigmentosum. Presented from the Barnard Free Skin and Cancer Hospital.

M. A., a white woman aged 28, began at the age of 2 years to have many freckles after exposure to sun and wind. When she was 4 years old, a definite diagnosis was made by Dr. Joseph Grindon Sr., and the patient was exhibited by him in Chicago. When she was 7 years old, the family moved to Oregon, and while there she was treated with ultraviolet radiation. This caused a generalized blistering, and the skin became much worse. At the age of 16 a nodule appeared on the right side of the nose, and this was removed with paste. The condition has become progressively worse, with "sores" forming at intervals, and there is no longer a seasonal variation. There has been no known intermarriage among her forebears. Her mother is healthy, has a few freckles and a thin skin. There are no sisters. She had 4 brothers. One of these had xeroderma pigmentosa and died at 27 from carcinoma, which developed at the site of one of the lesions. The others have a few freckles, but are normal and healthy. One brother has 2 children, who are normal and healthy. Recently the patient has had some difficulty with vision in the right eye. She is otherwise in good health, but is an uncooperative patient and comes to the clinic as long as a year after an ulceration develops. Recently she has taken no precautions to avoid sunlight and has been working in the field in the summer picking cotton, and she says this does not seem to make the disease progress more rapidly than usual.

The mucosal surfaces are normal, and she is apparently, apart from the eruption, in good health. Her skin in general is atrophic and of the sailors' skin type, with numerous deeply pigmented freckles of various sizes involving mostly the exposed surfaces. The scalp, axillas, soles, palms and pubic and inguinal regions are practically free. Several white scars of varying size are present, mostly on the face and upper extremities. There are small superficial ulcerations developing in a lentiginous border.

The Kahn test was negative. Roentgenograms of the lungs and long bones showed no pathologic change. Examination of the blood and urinalysis gave results within normal limits.

The biopsy specimen was taken from a pigmented nonulcerative lesion on the face. The epithelium showed marked hyperkeratosis. The rete pegs were hyperplastic, irregular and narrowed. There was marked deposition of melanin in the upper part of the corium. Moderate cellular infiltrate was present throughout the corium. Other biopsy specimens have shown squamous cell carcinoma, basal cell carcinoma, vascular pigmented fibroma, basosquamous cell carcinoma and melanoma.

Idiopathic Multiple Hemorrhagic Sarcoma. Presented from the Barnard Free Skin and Cancer Hospital.

B. P., a white man aged 62, first noticed a few nodules on his right foot four years ago. New lesions appeared on his leg and left hand. They were first red

and later bluish. No relative has ever had an illness similar to his. Multiple flat tumors are seen on both feet and the right leg. The lesions are soft and do not fade on pressure. They vary from 0.5 to 2 cm. in diameter. A histologic section showed some flattening of the rete pegs. Characteristic changes were seen in the corium, with proliferation of the small blood and lymph vessels, the presence of blood pigment in the tissue spaces and a moderate lymphocytic infiltrate. He has improved under roentgen therapy.

DISCUSSION

DR. E. B. TAUBER, Cincinnati: This case, I think the members all agree, is one of multiple idiopathic hemorrhagic sarcoma, but while a great many of the classic symptoms are present, some are absent.

The location on the hands and feet of bluish red bean-sized nodules with a doughy swelling, with telangiectases and tumors or an elephantiasis-like thickening, make a clinical picture all dermatologists agree on, but the histologic pictures have caused much disagreement and confusion.

Some agree with Kaposi, who found a round cell sarcoma with capillary hemorrhage; others, particularly Julius Dörffel, think the disease is one of the reticuloendothelial system, including a disturbance in its monocytogenic function which may terminate in true malignancy. Pautrier classified the disease as a neurovascular dysgenesis.

MacKee and Cipollaro have stated that Kaposi's sarcoma is caused by an unknown systemic agent that attacks the vascular apparatus, causing chronic hyperplastic inflammation and granuloma, and that the histogenesis is compatible with —and indistinguishable from—that of a neoplasm.

Campana, Semenow and Saphier found anatomic changes in the peripheral nervous system in some patients with Kaposi's sarcoma. They expressed the belief that a relation exists between Kaposi's sarcoma and the nervous system, without pretending that the new growths of this condition are nerve tissue. Other authors have stated that the cells comprising the tumor arise from the endothelium, and the name endothelioma was proposed; still others suggested names derived from other elements of the vascular wall, such as perithelioma, schwannoma and reticuloma.

The discussion today seems like carrying coals to Newcastle, as most of the members have, no doubt, seen the last issue of the *Journal of Investigative Dermatology* (**1**:379 [Oct.] 1938), in which S. W. Becker and H. W. Thatcher have published an article which is almost authoritative and gives a complete discussion of this condition. I agree with their conclusion, that it is probably a benign neoplasm with a multicentric origin and characterized by vascular proliferation and hyperplasia of spindle cells arising in perithelial tissue.

Perifolliculitis Capitis Abscedens et Suffodiens. Presented from the clinics of Washington University School of Medicine.

E. S., a Negress aged 31, five years ago began to have lumps on the scalp, some of which opened and discharged pus. These were not painful. A few months later lesions began to appear about the genitalia and in the axillas. Three years ago she presented herself for treatment, but since that time she has had a variety of other illnesses. The lesions on the scalp have slowly grown more extensive, while those in the axillas and groins have gradually cleared. Pustular lesions about the anus developed in 1936, and in February 1937 an anal fissure was excised. In September 1938 routine examination of the blood disclosed 4 plus reactions to the Wassermann and the Kline test. These had previously given negative results repeatedly, and the patient presented no other signs of syphilis. She had been told she had "scrofula" of the neck as a child. She has never had any symptoms of pulmonary disease, but has had an occasional attack of tonsillitis. An uncle died of tuberculosis, but there is no other familial history of disease.

On the scalp there are many areas of alopecia, which have apparently followed infections similar to that now present. The active lesions are papules and nodules,

which are inflamed and tender to the touch. The surfaces of many of them ooze and on pressure discharge purulent and seropurulent material. The surface of the scalp is irregular, owing to these infections in their various stages. Similar lesions, though less numerous, are present in the axillas and about the pubis. A few regressing lesions can be seen on the upper parts of the arms. Irregular sinus tracts and linear scars are present on either side of the anus.

The basal metabolic rate was —2 per cent. Cultures for fungi have been repeatedly negative, only Staphylococcus albus usually appearing. Blood counts have been essentially normal. Inoculation of a guinea pig showed no sign of tuberculosis. The gonococcus fixation test gave a 4 plus result in October 1938.

A histologic section from the scalp showed pathologic change throughout the whole slide. The most marked was that of a diffuse cellular infiltrate throughout the middle and lower strata of the corium and the subcutaneous tissue. This infiltrate was more dense in the glandular regions and involved the glandular structures and hair follicles. It was made up of lymphocytes, with an occasional polymorphonuclear leukocyte and a small amount of necrosis. The upper layer of the corium was relatively free.

Nothing has influenced the course of this infection very favorably. Local applications have not checked the spread of the disease. Courses of various staphylococcic vaccines have been given without great benefit. Intramuscular injections of manganese butyrate and injections of dermatomycol had little effect.

DISCUSSION

DR. THEODORE CORNBLEET, Chicago: According to a French view, perifolliculitis capitis abscedens et suffodiens is merely acne conglobata in a special location. Acne conglobata has supposedly a tuberculous background, which underlies the opinion held by some that perifolliculitis is a tuberculid, perhaps related to acne necrotica. In the patients I have seen, tuberculosis did not seem at all conspicuous as a factor; on the contrary, 2 of them were robust. The only type of organism in their lesions was a staphylococcus. Perhaps the simplest and most logical view is to consider perifolliculitis capitis a staphylococcic infection of an ordinary type on a poorly resisting soil. If the organisms are transplanted from the scalp to other parts of the skin nothing much happens. This disease responds only slowly to any of the ordinary applications used against the pyogens. Radiation and nonspecific agents appear to be more useful.

Fox-Fordyce Disease. Presented from the Barnard Free Skin and Cancer Hospital.

O. B., a Negress aged 30, noticed itching in both axillas and the pubic area about one year ago. Numerous hard dark papules are seen in these areas. Few lesions are present on the areolas. The lesions are smooth, shiny and firm. There is marked pruritus. Histologic section showed dilatation of the sweat ducts and cellular infiltrate about them and the hair follicles. The tubules of the apocrine glands showed parenchymatous degeneration. Treatment has helped little.

Keratosis Follicularis. Presented by DR. JOSEPH GRINDON and DR. JOSEPH GRINDON JR., St. Louis.

E. J. S., a white woman aged 23, was first seen in the office of the presenters in July 1938. She had noted for eight years a scaly condition of the skin. This became more prominent in warm weather.

Examination of the skin shows hyperkeratotic brownish gray flat pinhead-sized and smaller papules at follicular openings on the forehead, face, neck, shoulders, upper third of the back and extensor surfaces of the forearms. These lesions are best marked on the shoulders and upper part of the back, where there is mild pruritus. The scalp, axillas, groins and middle of the trunk are free. Keratotic

depressed plugs are present on the palms, soles and lateral aspects of the feet. Also, there are a few groups of small discrete vesicles on the fingers.

General physical and laboratory examinations gave essentially negative results.

Histologic examination showed a pathologic picture typical of keratosis follicularis, with much dyskeratosis and many *corps ronds.*

Apparent improvement has followed roentgen therapy, 88 roentgens being given every two weeks.

DISCUSSION

DR. HARTHER L. KEIM, Detroit: I think the members are all agreed that this condition is a mild example of keratosis follicularis. Furthermore, the microscopic picture with its characteristic epithelial changes and follicular plugging removed any possibility of doubt concerning the classification of this dyskeratosis. Shown here with unusual clarity were great numbers of the degenerated epithelial cells which Darier thought were psorosperms and which he mistakenly identified as the causative factor. In spite of the fact that this somewhat rare disease was first described by Morrow in 1886 and a few years later was thoroughly investigated by Darier, dermatologists must still say with Haase "etiology unknown."

A number of writers have called attention to several cases occurring in the same family, but there is little else to support a theory of familial causation.

Since nothing is known as to the cause of keratosis follicularis, therapy has in general been limited to keratolytic applications and local destructive measures. Filtered roentgen rays enjoy some reputation in reducing the hyperkeratotic infiltrate. Since, as with acne vulgaris, the process originates in the pilosebaceous apparatus and since therapeutic efforts with the glandular preparations are achieving some measure of success in the treatment of acne, it is within the realm of possibility that the endocrine approach may have something to offer in this syndrome, whose cause is still unknown.

Localized Amyloidosis Cutis. Presented from the Barnard Free Skin and Cancer Hospital.

C. F., a white man aged 71, has had itching of both legs for the past seven years. The eruption is located on the shins and consists of irregular patches of hyperkeratotic elevated lesions that feel rough. The skin between them is hyperpigmented. Intracutaneous injections of congo red caused staining of the elevated lesions, which remained pink for several weeks. A frozen section of one of these areas showed amyloid in the papillary bodies. The itching was somewhat relieved by roentgen therapy.

DISCUSSION

DR. O. S. PHILPOTT, Denver: To open the discussion of the case of localized amyloidosis cutis, several points of similarity between it and a case which Dr. A. W. Freshman and I reported (ARCH. DERMAT. & SYPH. **33**:971 [June] 1936) should be mentioned. In both, the eruption began insidiously and itched intolerably from the beginning. Local applications were entirely ineffective. In our case there was but slight tendency to coalescence of the individual lesions, which may be accounted for by the fact that the eruption was of less than two years' duration. In both cases study of tissue and staining, including subcutaneous vital staining with congo red, established the diagnosis, but biopsy alone would not have been sufficient. The condition in both cases comes under the category of primary cutaneous amyloidosis, but in ours there was active pulmonary tuberculosis of many years' duration, a fact which should be considered in attempting to formulate some ideas regarding the pathogenesis.

The presenters should be complimented for carrying out the necessary investigations to establish a diagnosis in this condition, which otherwise would have been accepted clinically as another case of lichen chronicus simplex or lichen planus hypertrophicus.

Acrocyanosis. Presented from the Barnard Free Skin and Cancer Hospital.

M. R., a white woman aged 53, noticed three years ago that her fingers were blue. The discoloration was periodic, coming on several times a day, and increased in severity. It was worse when her hands were cold, as after being in cold water or after exposure in winter. In cold weather she frequently had attacks twenty or more times a day. In the past year her hands have become numb, and she has been unable to use them during the attacks. An attack usually lasts about fifteen minutes and is followed by pain similar to that caused by frostbite. In the past year the feet have swelled occasionally but have never turned blue. Two brothers

Fig. 5.—Amyloidosis cutis.

and 1 sister died of tuberculosis. The patient does not use tobacco, alcohol, snuff or drugs. There are no recent symptoms of tuberculosis, but years ago she spent three months at absolute bed rest after hemoptysis. In 1935 a squamous cell carcinoma of the cervix was treated in the Barnard Free Skin and Cancer Hospital by roentgen and radium irradiation and an abdominal operation.

The hands are cold; hyperhidrosis and cyanosis are present from the first interphalangeal joint to the tip of each finger. The fingers are cracked and fissured with a tendency to clubbing. There is slight edema of the feet but no cyanosis. The patient was exposed to cool air for fifteen minutes. After this a marked bluish cyanosis appeared on the distal phalanges, gradually faded out

toward the hands and stopped at the wrists. The hands became cold, swollen and clammy. Then the wrists were placed for fifteen minutes in water at 20 C. They merely became bluer. When they were placed in water at 10 C., there was pain, described as a sensation of stiffness and pinpricking. They then became deeper blue, with bright red spots scattered throughout. Then they were placed in water at 42 C., and as they warmed they exhibited a reactionary hyperemia, becoming orange-red.

The circulation of a finger was occluded by a rubber band and the reactionary hyperemia, after removal of the band, extended 2 cm. proximal to the constriction. (In controls the reactionary hyperemia stops at the line of constriction.) A cyanotic area may be blanched by pressure; the return of color, however, is only from the periphery and not from the center and the periphery, as might be expected. Immersion of the hands in water at different temperatures caused no change in the brachial blood pressure, which was 128 systolic and 80 diastolic; only cyanosis of the hands and fingers appeared, lasting about fifteen minutes. The radial pulse is good. There is slight pitting of the feet to the ankles. The posterior tibial arteries are palpable. There was no reaction of cyanosis to cold in the feet as in the hands.

The Wassermann and the Kahn test were negative. The blood picture was normal. The basal metabolic rate was —13 per cent. The blood sugar during fasting was 90 mg. per hundred cubic centimeters of blood, and the urea nitrogen 10 mg. The arterial blood had an oxygen content of 15.5 volumes per cent and a capacity of 16.1 volumes per cent; the venous blood, a content of 8 volumes per cent. Roentgenograms and laminagrams of the chest demonstrated fibrosis of the apexes, with small cavities at the periphery of the upper part of both pulmonary fields.

The condition clears spontaneously on absolute bed rest, but even then will appear if the hands are put in ice water. Treatment has been supportive, but in spite of this the disease has continued to progress.

Dermatitis Rupioides Arthropathica. Presented by DR. NORMAN TOBIAS, St. Louis (from Firmin Desloge Hospital).

R. K., a white woman aged 45, has had arthritis for seven years. The ankles have occasionally been swollen during the past two or three years. There is occasional stiffness of the neck and shoulders. Eight months ago the fingers became stiff and deformed. The eruption first appeared on the fingers and toe nails six months ago. About six weeks ago the eruption appeared on the knees, ankles and lower portions of the legs.

Examination of the skin shows numerous thick yellow-crusted pustular lesions about the ankles and knees. Removal of the crusts leaves a beefy surface. Subungual hyperkeratoses of the big toes and a hyperkeratotic condition of the fingers are present. The fingers, feet and toes are flexed and immobile.

The gonococcus fixation test gave a negative result. A smear from the under surface of the biopsy specimen and repeated smears and cultures from the cervix uteri have been negative for gonococci. The Kahn, the Kline and the Wassermann test were negative.

Histologic study showed decided parakeratosis, with slight hyperkeratosis, acanthosis with intracellular and intercellular edema and marked edema of the cutis with a scattered perivascular infiltrate consisting of lymphocytes, polymorphonuclears, plasma cells and a few eosinophils.

Recalcitrant Pustular Eruption of the Hands and Feet. Presented by the Clinics of Washington University School of Medicine.

M. W., a Negro aged 35, noticed pustules appearing on the hands in June 1938. A week later they appeared on the feet, and the skin on both areas became so dry and scaly that movements of the joints were limited. He has lost 20 pounds

(9.1 Kg.) since June, but there are no pulmonary symptoms. He has had gonorrhea for fifteen years and last September had acute gonorrheal urethritis for about four weeks. He works as a porter and states that just a few days before the eruption began he was employed in washing walls with a cleaner and a solution of household lye.

His prostate is moderately enlarged, and on massage yields clear white fluid, which shows only a few pus cells and gram-positive cocci.

The nails of the hands and feet are normal. There is a pustular eruption of the palms and fingers and the dorsa and sides of the feet. These pustules vary in size from that of a pinpoint to that of a split pea. They contain creamy pus, which on microscopic examination shows extremely sparse leukocytes and a few tiny short chains of streptococci. The epidermis is thin and glistening, with numerous fissures and scaliness at the edges of the lesion. The palms and all surfaces of the fingers are affected. The dorsa and sides of the feet are involved, but the soles are free. There are scaly patches along the upper third of each forearms, over the superficial portion of each ulna. There are also a few similar isolated scaly patches on the legs, thigh and penis. There are no pustules in the latter areas.

The Wassermann, the Kahn and the Kline test have all been negative repeatedly. Culture of material from the pustules showed no gonococci. A microscopic section from the skin of the right leg near the ankle showed two intraepidermal abscesses with well marked borders, their bases being demarcated by a zone of epithelial cells. There was a thin crust over the upper surface. The abscesses were composed of polymorphonuclear leukocytes. A few small areas of infiltrate in the corium were made of lymphocytes.

Various antiseptic ointments and hot compresses have been applied without much benefit, and recently the skin of the legs and thighs has become involved in several small patches.

DISCUSSION

Dr. George C. Andrews, New York: Clinically and histologically this condition is not at all like pustular bacterid or pustular psoriasis. The lesions in this case are on the dorsa of the feet, with practically no involvement of the soles, and there is an involvement of the toes which is not seen in pustular bacterid. Also, the patches on the palms are not as well defined as the ones in pustular bacterid usually are. Histologically in this case there was a superficial pustulovesicle, truly an impetiginous type of lesion different from that described in pustular psoriasis and in pustular bacterid, in which diseases the abscesses are deep in the epidermis or are subepidermal.

With these facts in mind, namely, that the histologic structure in this case was that of an impetiginous, superficial pustulovesicle and that a streptococcus was grown on culture, the possibility of a streptococcic acrodermatitis such as Mitchell described should be kept in mind. I do not think that diagnosis can be settled on, because the streptococcus obtained was a short chain streptococcus and may be of no importance. However, I think these cultural studies should be continued.

Seborrheic Keratosis (with Carcinomatous Change). Presented from the Barnard Free Skin and Cancer Hospital.

N. S., a white man aged 86, has noted scaly brown areas on his face and back for thirty years. These have slowly enlarged, and new lesions have appeared. About two years ago several began to ulcerate. The patient has lived in the city for twenty-four years, having been a farmer previously. There is no history of arsenical ingestion. The back, chest and face are studded with soft pigmented verrucous keratoses, varying from 1 to 8 cm. in diameter. The ulcerated lesions on his chin and back have pearly borders. Histologic section of these lesions showed basal cell carcinoma.

DISCUSSION

DR. E. A. OLIVER: While seborrheic keratoses are common in older persons, carcinomatous changes in them are rare, especially in lesions on the covered parts. In an excellent article J. J. Eller and V. J. Ryan (ARCH. DERMAT. & SYPH. **22**:1043 [Dec.] 1930) pointed out the essential clinical and histologic differences between seborrheic and senile keratoses. They stated the belief that they had seen basal cell epithelioma develop in lesions on the face, but never in lesions on the covered portions of the body; in closing the discussion of their paper, Eller cited Satenstein as saying he had seen basal cell epithelioma develop from lesions of this type on the covered portions of the body. J. Jadassohn and Bruno Bloch, however, stated that they had never seen epithelioma, even of the basal cell type, develop, even on the face.

While the lesions on the trunk are unmistakably those of seborrheic keratoses, it is often difficult to differentiate them from senile keratoses when both are present on the face. Generally a biopsy is necessary.

Contact Dermatitis (Ragweed). Presented from the Barnard Free Skin and Cancer Hospital.

J. F., a white man aged 30, has had an eruption each summer for the past seven years. It usually begins in May or June and lasts until October, although this year it has lasted until November. There is a family history of allergy. The patient had hay fever each summer until three years ago. It has not been noted since. There is decided pruritus with the eruption, which is present on the forearms, legs, especially in the flexural folds, neck and forehead. Numerous tiny excoriated papules are seen, with some erythema and scaliness. Patch tests with oil of dwarf and giant ragweed for twenty-four hours produced a violent reaction. This was accompanied with a focal flare-up. Intramuscular injections of a 3 per cent (by volume) suspension of dwarf ragweed oil in almond oil are being given, and the patient is gradually improving. He usually gets well at this time of the year. The patient is shown with positive reactions to patch tests on his arm.

DISCUSSION

DR. MARION B. SULZBERGER, New York: The subject which this case brings up for discussion is perhaps of more practical importance than any or even all of the others presented at this meeting.

In principles of pathogenesis, the contact type of dermatitis due to ragweed is in all probability no different from allergic occupational dermatitis of contact type, which accounts for over half of all occupational diseases and runs into many millions of dollars of annual costs in this country. It is not different from the thousand and one other varieties of allergic contact type eczematous dermatitis from clothing, cosmetics, topical medicaments, disinfectants, insecticides, anesthetics and other plants. All these allergic contact eczemas are in turn probably not different in pathogenesis from all the various types of allergic eczematous responses to micro-organisms, as seen, for example, in eczematous dermatophytosis and in eczematous dermatophytids.

For this reason, any method efficacious in one form of contact type dermatitis may be expected to be applicable to other forms as well. It is therefore most imperative to try to decide whether or not specific treatment by means of intramuscular injections of oil fractions of plants actually does reduce the skin's level of sensitivity. The members all know that there is radical disagreement among various observers on this most fundamental question.

I am of the opinion that much further study would be required in this particular case of Dr. Kile's to prove that any beneficial effects had occurred from injection of ragweed oil. However, since Dr. Fred Wise and I first attempted desensitization in ragweed dermatitis (*J. A. M. A.* **94**:93 [Jan. 11] 1930) I have observed a fair number of instances in which the clinical benefits obtained from injections of the plant oils appeared to me so evident as to be beyond reasonable doubt. Several of these were cases of ragweed dermatitis and several cases of

dermatitis due to chrysanthemum, tulip, gallardia, tobacco and other plant oils, under conditions of quantitatively controlled repeated clinical exposures. However undeniable these clinical effects seemed to be, in many other cases, both of my own observation and in the literature, specific desensitization seemed of little or no avail.

In view of these contradictory findings and opinions, it seemed essential to find an objective method of determining whether the degree of sensitivity of the skin had been reduced by the specific measures. My collaborators and I have attempted to study this question by means of quantitative patch tests with serial dilutions of the plant oil before the institution of the specific injections and thus determining the degree of preexisting sensitivity. After completion of the series of specific injections, the same serial dilutions were applied for quantitative patch tests, and the new degree of cutaneous sensitivity was thus determined. With this objective method, Dr. Greenberger, Miss Malozzi and I were not able to demonstrate in a large series (several hundred) of subjects treated with ivy oil that the injections produced any uniform reduction in the level of the skin's sensitivity to patch tests with the substance.

However, one must bear in mind that the patch test with oil extract as we performed it cannot be regarded as the absolute equivalent of clinical exposure to the plant. Moreover, as Dr. Hans Field and I showed (*J. Allergy* **7**:139 [Jan.] 1936)—and my collaborators and I have since confirmed the point in many cases—repeated quantitative patch tests are not necessarily reliable, as the results are too much subject to the influences of the not uncommon sharp (spontaneous), chronologic and local variations in the level of the skin's sensitivity. Furthermore, one must consider the effect both of the dermatosis and of the first patch tests, as well as chance intercurrent specific and nonspecific influences, when comparing the level of the reactions to the second and the first series of tests.

If I should be forced to express an opinion on this whole important subject, I could say only that I am as yet unable to make up my mind as to whether the efficacy of desensitization with plant oil is established in principle. My own clinical observations are themselves contradictory. However, I believe that I may conclude that in some cases, provided the right extract is properly given and the patient is in a state of allergic equilibrium which lends itself to hyposensitization, the specific measures achieve a sufficient reduction of cutaneous sensitivity to afford a manifest prophylactic effect—always provided that the clinical exposures are not too massive.

Much more work is required on this to my mind superlatively important and urgent problem; above all, modifications of cutaneous testing methods are needed which will make possible objective determination of whether the treatment administered is accomplishing a reduction in the degree of eczematous sensitivity. Planned and controlled experiments with variations in extracts and routes of administration might then eventually result in the discovery of specific methods of immunization against eczematogenous allergens and thus prevent a large number of different forms of allergic eczematous dermatitis of contact type.

NEW YORK DERMATOLOGICAL SOCIETY

J. Frank Fraser, M.D., *President*

Dec. 20, 1938

Frank C. Combes, M.D., *Secretary*

A Case for Diagnosis (Lymphangioendothelioma? Angioma?). Presented by Dr. Fred Wise.

W. C., a baby aged 3 weeks, was registered at the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital on Dec. 20, 1938, with a lesion on the left buttock of two weeks' duration.

On the midarea of the left buttock there appeared, about a week after birth, a hemispherical tumor about the size of a golf ball. The edges were sharply outlined and the surface adherent to the overlying skin, but the mass was movable with the surrounding normal tissue. Its color was a faint bluish pink; otherwise the overlying skin was unaltered. On palpation a firm, nonfluctuating and nontender mass was felt. The mother states that the tumor has seemed to be enlarging rather rapidly in the past two weeks.

DISCUSSION

Dr. Howard Fox: One should consider the possibility of subcutaneous adiponecrosis of the newborn, though the picture is not classic. There is only one lesion, whereas in all the cases I have observed the eruption was bilateral. The small size of the lesion would not militate against this disease, as in some cases there are only pea-sized to bean-sized lumps on each cheek. The differential diagnosis between subcutaneous fat necrosis and angioma of some type should be settled within four or five months, as angioma lasts for years. One point against the diagnosis of subcutaneous fat necrosis is that the baby was small at birth and labor was not difficult. She was, however, the first child.

Dr. George M. MacKee: I doubt that this condition is adiponecrosis, because of the color. I think in most cases of lesions due to fat disturbance the overlying skin is tense and shiny and rather waxy in appearance, with no color. Here are a red center and a bluish periphery. An angioma can produce a sharply circumscribed tense subcutaneous lesion with bluish and reddish discoloration of the surface. Some such lesions are a mixture of angioma and fibroma, and that is my tentative diagnosis.

Dr. Edward R. Maloney: I agree with Dr. MacKee about this condition's not being fat necrosis, for the same reasons, and I agree with his diagnosis, but I should say fibroangioma, because the fibrous element in this lesion seems to me to be greatly in excess of the angiomatous element. I should make the diagnosis of fibroangioma.

Dr. A. Benson Cannon: I think, as do the previous speakers, that this lesion is a fibroangioma, and perhaps traumatic in origin. I should expect it to disappear spontaneously in a few months. I think that the growth is comparable to the swelling that one often sees after injections of some irritating substance. I have seen just such a tumor with a hemorrhagic center following an injection of a bismuth or a mercury preparation. Such nodules usually disappear in six or eight months.

Dr. Eugene F. Traub: I believe that it is not fat necrosis, for the reason stated by Dr. MacKee and also because the surface seems soft, whereas induration is to be felt in the deeper portion. In the cases of fat necrosis that I have observed the induration has been dense from the surface of the skin down. The central red portion of this lesion suggests an ordinary angioma to me, and underneath this there is a zone in which a purplish discoloration shines through the skin, and I believe this represents a cavernous angioma. I am not certain as to the extent of the fibromatous element, and I believe the entire lesion is vascular, with perhaps some inflammatory reaction accounting for some of the induration.

Dr. Frank C. Combes: My conception of this case is that mentioned by Dr. Cannon, namely, that the lesion is traumatic in origin. I should advise against any treatment because I do not think it will respond to anything except excision and there is a strong possibility that it may disappear in much the same way fat necrosis disappears.

Dr. Paul E. Bechet: The baby is 3 weeks old, and the lesion has been present for two weeks, according to the mother. Dr. M. M. Estrin, of the staff of the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hos-

pital, has seen the baby for the past two weeks, and he says the lesion has increased rapidly in that time. It seems incredible that a fibroangioma would increase so quickly. I believe that the lesion is an angiosarcoma.

DR. R. H. RULISON: I was inclined to think this a mixed angioma, along the lines suggested by Dr. Traub, rather than those suggested by the other speakers. I mean by that that it has both capillary and larger vascular elements underneath, and I think it happens to have a dense capsule. I think it is angioma rather than fibroangioma.

DR. HOWARD FOX: I should like to ask Dr. Traub, who has made a special study of nevi, whether he thinks a fibroangioma would disappear in a few months.

DR. EUGENE F. TRAUB: I did not get the impression that this lesion would disappear in that way. If it is a cavernous angioma, the likelihood of a spontaneous disappearance is not great. No doubt an angiosarcoma may appear anywhere, but I should not expect it in that locality. From the perusal of the literature, I should judge that the occurrence of an angiosarcoma in that locality would be exceedingly rare.

A Case for Diagnosis (Keratoderma Palmare et Plantare? Eczema? Tinea?). Presented by DR. J. FRANK FRASER.

F. B. M., a woman aged 64, when seen in 1935 presented an area of lichenification over the right instep. After roentgen therapy the eruption disappeared. She returned in April 1938, with an eruption which showed scaling and fissures on the palms and soles. For this condition she was given seven ¼ erythema doses of roentgen rays, with apparent improvement. During the month of October the feet became painful, and the skin of the soles exfoliated. She was confined to bed for five weeks, with severe pain in the feet. After the peeling of the skin from the soles, the condition appeared to be greatly improved, but the improvement did not last and the patient is now suffering from a relapse.

Chemical examinations of the blood gave normal results. The blood count showed 42 per cent polymorphonuclear leukocytes, 40 per cent lymphocytes and 11 per cent eosinophils.

DISCUSSION

DR. R. H. RULISON: I should like to ask whether any investigation has been made of the possibility of arsenical keratosis.

DR. J. FRANK FRASER: The patient states that there has been no ingestion of arsenic or of any other drug.

DR. GEORGE M. MACKEE: I cannot help much. I should think, diagnostically, first of the possibility of a hyperkeratotic type of dermatomycosis. I think, also, it is necessary to rule out the possibility of psoriasis. As for suggestions for treatment, I think one should try to prove the diagnosis first by mycologic examination, cutaneous testing and perhaps biopsy. Then one might make more intelligent therapeutic suggestions.

DR. EUGENE F. TRAUB: The question of an acquired type of keratosis has been raised, and I believe that is one diagnosis which can be excluded on clinical grounds alone in this case. My reason for this statement is that ordinary keratoderma of the sole spares the instep, while the weight-bearing areas are particularly affected. The reverse is true in this patient, who presents most of the eruption on the instep, while the weight-bearing areas are spared. There are other reasons in this case for excluding keratoderma. As Dr. MacKee suggested, I should first consider some type of tinea, and if that diagnosis can be excluded after thorough microscopic and cultural studies, my next choice would be psoriasis.

DR. FRANK C. COMBES: I agree with everything Dr. Traub has said regarding acquired keratoses. I suggest laboratory investigations to prove the diagnosis. Otherwise the treatment is necessarily empiric. I suggest the use of 20 per cent barium sulfide in zinc oxide ointment. Care must be taken in its application. It will take off the scales and soften the lesion better than anything else.

Lupus Vulgaris and Pulmonary Tuberculosis. Presented by Dr. Howard Fox.

Mrs. B. V. S., aged 25, first noticed an eruption eleven years ago. The first patch appeared on the buttock and was gradually followed by four others within two years. She now presents sharply circumscribed patches varying in size from that of a pea to that of a palm. They consist of apple jelly nodules and are typical of the flat nonulcerating type of lupus vulgaris. They are situated on the right nostril, each knee, the left side of the trunk and the right buttock. The mucous membranes are free.

At the age of 17 (eight years ago) she had pneumonia, followed by pulmonary tuberculosis. She was treated for seven years in a sanatorium in Denver, where thoracoplasty was performed. The pulmonary tuberculosis is still somewhat active, as shown by the occasional presence of tubercle bacilli in the sputum. The patient is well nourished and does not look ill. There is no history of tuberculosis in her family. The lupus vulgaris was treated unsuccessfully by a salt-free diet.

DISCUSSION

Dr. Frank C. Combes: I agree with the diagnosis. It is exceedingly unusual for a patient to have lupus vulgaris and active pulmonary tuberculosis simultaneously.

Dr. George M. MacKee: Dr. Fox presented the patient for that reason. It is unusual, if not rare, for a patient to have lupus vulgaris with active pulmonary tuberculosis. I think I saw practically all the dermatologic patients at Saranac Lake, N. Y., over a period of eight years. I saw a few patients with lupus erythematosus, granuloma annulare, tuberculosis verrucosa cutis, orificial tuberculosis and sarcoid, but not a single patient with lupus vulgaris.

Dr. A. Benson Cannon: I also think the combination of pulmonary and cutaneous tuberculosis is unusual. The question that is most interesting to me is whether lupus vulgaris with active pulmonary tuberculosis should be treated at all. Why not treat the patient's pulmonary tuberculosis and let the benign tuberculosis of the skin alone? When treatment of the cutaneous tuberculosis is indicated, I have noticed that small doses of arsphenamine give good results. Many lesions such as this patient presents are apt to disappear after the use of arsphenamine.

Dr. Eugene F. Traub: Dr. Fox did not state whether he wished therapeutic suggestions for the treatment of the cutaneous lesions in this case, but as I just had a patient who had a large number of scattered patches of lupus vulgaris that were cured by surgical treatment, I cannot help mentioning this. The outlook for my patient seemed absolutely hopeless because of the great number of lesions and their rather wide extent. Most of the local measures used on the skin had proved utterly inadequate. About three fourths of the scalp had been involved, and the process had begun to spread toward the face. All the patches were surgically excised and skin was grafted, with a most excellent result. Apart from the fact that the local disease appears to be cured at the present time, the psychologic effect of the removal of the various spots was even more remarkable. While the patient under discussion presents as the chief problem the pulmonary tuberculosis, which naturally should be given primary attention, I see no reason why the local patch should be allowed to spread or the patient should be allowed to get others if this might be prevented. There certainly could be no contraindication to removing the patch under local anesthesia. My patient has now gone a little over a year with no recurrence at any of the sites of excision.

Dr. Fred Wise: Does Dr. Traub recommend that a discoid patch 4 or 5 inches (10 to 13 cm.) in diameter be excised?

Dr. Eugene F. Traub: When large patches are removed surgically, no attempt need be made to bring the edges together. Tiny pinch grafts may be employed or the entire area covered with a large Thiersch graft.

DR. J. FRANK FRASER: Dr. Fox presented the case because of the rarity of the association of pulmonary and cutaneous tuberculosis. Pulmonary tuberculosis is common; lupus vulgaris is rare in this country. Dermatologists would see lupus vulgaris more frequently if it were a secondary condition. What then is the pathogenesis of lupus vulgaris? Aschoff expressed the belief that it develops from a primary focus left over from the tuberculosis which he said every one has had during childhood. This theory is not universally accepted. Hamilton Montgomery (ARCH. DERMAT. & SYPH. **35**:698 [April] 1937) stated: "Lupus vulgaris is essentially inoculation tuberculosis." Treatment in a sanatorium should be the method of choice.

DR. HOWARD FOX: Pulmonary tuberculosis may occur simultaneously with certain types of cutaneous tuberculosis. The occurrence, however, of lupus vulgaris with tuberculosis of the lungs is distinctly rare. I do not think treatment of the lupus is indicated, except for the lesion on the ala nasi, which should be treated on account of the possibility of extension to the mucosa.

Lichenoid Eruption of Zosteriform Distribution. Presented by DR. HOWARD FOX.

Mr. J. J., a salesman aged 39, contracted syphilis in 1931. He was adequately treated, and his Wassermann reaction was negative at the last determination. The last injection of any type of arsenical preparation was given on Jan. 12, 1938, at which time he received 0.04 Gm. of mapharsen. This was followed a few days later by a patchy eczematous eruption, which lasted a few weeks. All of the eruption disappeared except two oozing crusted reddish patches the size of a silver dollar, one in the suprapubic region and one at the root of the penis. Three months ago an eruption of zosteriform distribution began to develop, new lesions continuing to appear until recently. The eruption is situated on the right side of the chest, the anterior axillary fold and the internal aspect of the right arm and forearm. The lesions are dry scaly well defined plaques the size of small coins. The color is suggestive of lichen planus, but there are no individual papules characteristic of this disease. On the mucous surface of the right commissure of the lip is a small patch consisting of aggregated grayish white pinhead-sized lesions. From January 1938 until the onset of the lichenoid eruption he received intramuscular injections of mercury and bismuth preparations. He has taken no other drugs. Subsequent to the appearance of the lichenoid eruption he was treated with acetarsone for amebic dysentery.

DISCUSSION

DR. GEORGE M. MACKEE: I think the eruption is most likely annular lichen planus. Probably the patch on the mucous membrane of the lower lip is lichen planus also. I do not think it is an arsenical eruption. I do not think it has any relation to the treatment or to the original disease. The pubic lesion is probably an exudative eczema of unknown cause.

DR. EDWARD R. MALONEY: I agree with what Dr. MacKee has said. The most likely diagnosis here is lichen planus. The lesions on the arm, in my opinion, have nothing to do with the treatment or with syphilis. I do not know what to say about the lesion on the pubes, but the best diagnosis I can think of is an exudative dermatitis of some kind. The eruption definitely covers areas of skin that come together when he bends over, and there seems to be some sort of infectious element. Just what it is I do not know. I think it has nothing to do with the lichen planus and nothing to do with syphilis.

DR. A. BENSON CANNON: I agree with the previous speakers that the case is one of lichen planus.

DR. EUGENE F. TRAUB: Reversing the reasoning process, in any number of cases of syphilis treated with much arsenic, regardless of the time element, an eruption may have developed which resembled lichen planus. Exudative types of

eruption also are seen. The one diagnosis that would best suit this picture, therefore, is an arsenical eruption due to previous treatment. This would explain not only the lichen planus-like eruption on the arms, but would account perfectly well for the exudative eruption in the genital areas.

DR. FRANK C. COMBES: I agree entirely with Dr. Traub. I do not think this eruption is lichen planus. It is not typical of lichen planus, and the zosteriform distribution is not that of lichen planus. I do not see how one can get away from the arsenical medication. Arsenic will cause a lichen planus-like eruption with a histologic picture the exact counterpart of lichen planus.

DR. GEORGE M. MACKEE: As far as clearing up this diagnosis by histologic examination is concerned, that is doubtful because in the lichen-like eruptions apparently due to arsenic, the histologic changes have been those of lichen planus. I have seen supposedly arsenical lichen planus in a number of cases. The eruption has always been on the skin and never on the mucous membrane. This patient has a lesion on the mucous membrane that looks like lichen planus.

DR. FRANK C. COMBES: I meant that this condition is not the clinical entity known as lichen planus. I agree with Dr. MacKee that lichen planus following arsenic is the same as true lichen planus histologically. The zosteriform distribution here presented does not occur in true lichen planus but may be due to arsenic, which is neurotoxic. In answer to Dr. MacKee, I have never seen papules of lichen planus on the mucous membranes in a case of lichen planus-like eruption following arsphenamine medication.

DR. J. FRANK FRASER: Pigmentation occurs in lichen planus regardless of whether patients have been treated with arsenicals. The histologic picture of the so-called lichen planus-like eruptions following arsenical medication, in my experience, was typical of lichen planus.

DR. HOWARD FOX: Although I think this eruption is probably lichen planus, it is unusual for that disease to assume a zosteriform distribution.

Lupus Miliaris Disseminatus Faciei. Presented by DR. EUGENE F. TRAUB.

M. V., a woman aged 39, has been under treatment at the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital since August 1938, because of an eruption which she stated had been of one year's duration. The patient presents grouped papules varying in size from that of a pinpoint to that of a pinhead, some of them seeming to contain a tiny dot of pus and others seeming merely to have softening centers. On diascopic pressure the lesions blanch out flat and show a yellowish brown color typical of the so-called apple jelly appearance. Antisyphilitic treatment has had no effect on the eruption. The Wassermann test was negative to doubtful; the Kahn test was 2 plus. Urinalysis showed no abnormality except a trace of albumin. The tuberculin test was negative with dilutions of 1:1,000,000, 1:100,000 and 1:10,000.

A biopsy specimen was taken and showed folliculitis tuberculid histologically. The section showed a dense nodule about the hair follicles. The upper part of the corium was not involved. The cellular exudate consisted of round cells with some necrosis. There was no evidence of endothelioid cells or of the pathologic picture of tuberculosis.

DISCUSSION

DR. J. GARDNER HOPKINS: I do not see how one can make the diagnosis of lupus miliaris in the absence of tuberculous histologic changes, though one may make a diagnosis of Lewandowsky's rosacea-like tuberculid. The changes seem to me to fit better clinically into the latter picture.

DR. EDWARD R. MALONEY: I think that both clinically and histologically the condition is not lupus miliaris disseminatus faciei. It has not any of the clinical

features of that disease. It has not the pathologic picture of that disease. To me it seems to be bilateral, appearing on both cheeks and nowhere else on the face. That is unusual for lupus miliaris disseminatus faciei. It has the clinical appearance of a follicular necrotic acne-like eruption, and I think that is exactly what it is. It is some type of folliculitis and is not tuberculous or a tuberculid of any kind.

DR. GEORGE M. MACKEE: I think this case might be one of Lewandowsky's rosacea-like tuberculid rather than lupus miliaris disseminatus faciei, because of the flush and the symmetry, besides the small size of the nodules plus the unsatisfactory histologic picture. Lupus miliaris disseminatus faciei is supposed to have a much more definite tuberculoid structure than tuberculid. The tuberculin reaction is apt to be positive in cases of tuberculid and negative in those of miliary lupus, but in individual cases exactly the opposite state may exist. I rather lean toward Lewandowsky's tuberculid.

DR. FRED WISE: I am in agreement with Dr. MacKee's opinion.

DR. J. FRANK FRASER: Neither the clinical picture nor the histologic report read by the presenter in my opinion shows diagnostic features of lupus miliaris disseminatus faciei. Another biopsy should be performed.

DR. EDWARD R. MALONEY: I should like to ask a question of those who think this lesion is rosacea-like tuberculid: How can you call anything tuberculid if there is no evidence of tuberculid? There was nothing in the histologic picture to show any type of tuberculoid structure or tissue.

DR. EUGENE F. TRAUB: This patient has been under observation for between five and six months. The process at the present time, therefore, is practically in the healing stage. The patient should have been presented at an earlier meeting, but unfortunately she was unable to get here before today. The smallest size biopsy punch was used, and it may be that the characteristic portion of the lesion was not included in the specimen. The report on the tissue did not make an absolute diagnosis and, of course, did not exclude the possibility of tuberculosis of the skin. It would be exceedingly unusual for a woman of 39 years to have any type of pustular acne due to the acne bacillus producing this acute process, which on diascopic pressure looks as typical and characteristic of an apple jelly nodule as any I have seen. In fact, this patient has been used repeatedly to demonstrate to my class what a typical apple jelly nodule looks like. In the differential diagnosis rosacea-like tuberculid and lupus milaris disseminatus faciei were considered, and it was only on the basis of the clinical appearance that the latter diagnosis was suggested as the more likely one.

A Case for Diagnosis (Lichenoid Sarcoid?). Presented by DR. A. BENSON CANNON.

M. R., a housewife aged 39, was first seen in the Vanderbilt Clinic on Dec. 7, 1938, when she gave a history of the gradual development of an eruption on the neck, body and upper parts of the thighs for the past four and one-half months. There was slight itching. Eight years ago the patient was operated on for an ovarian pregnancy. Two years ago she received radium treatment and has not menstruated for the past ten weeks.

On the trunk, symmetrically reaching down the back to the sacral region, and on the flanks, around the neck and on the abdomen and upper parts of the thighs is an eruption composed of papules varying in size from that of a millet to that of a split pea. Some are follicular; all are yellowish. Some of the papules are flat topped, shiny and firm, with a tendency to grouping in clusters. The smaller lesions have central pinpoint-sized depressions, which apparently represent the opening of the follicle. There are no lesions on the face or in the mouth. When the patient was seen on December 9, mild spreading was noted on the inner aspects

of the lower parts of the thighs. The lesions on the chest and neck were flatter than those on the abdomen and showed perhaps some atrophy and sometimes a tendency to coalesce and form larger plaques.

The Kline and the Wassermann reaction were negative. Examination of the urine showed an alkaline reaction, a 1 plus reaction for albumin, no sugar, a few triple phosphate crystals, rare white blood cells and saturation with amorphous phosphates. The blood count showed 78 per cent hemoglobin, 5,350,000 red cells and 11,100 white cells, with a differential count of 54 per cent polymorphonuclear leukocytes, 29 per cent small and 1 per cent large lymphocytes, 6 per cent monocytes, 1 per cent basophils and 9 per cent eosinophils. The report on the biopsy showed tuberculoid infiltration with a tentative histologic diagnosis of miliary lupoid.

DISCUSSION

DR. FRED WISE: I probably should not have made the correct diagnosis clinically at first sight, but after being reminded that there is such a thing as lichenoid sarcoid, I think this example is the best one of that condition I have ever seen.

DR. PAUL E. BECHET: It is an interesting fact that an increasing number of lesions with no clinical resemblance to Boeck's sarcoid have been presented as that disease, the diagnosis being made on histologic grounds alone. If the histologic diagnosis is absolutely accurate the clinical conception of the disease will have to be changed radically.

DR. J. FRANK FRASER: If there is such an entity as lichenoid sarcoid, with the histologic picture showing a sarcoid structure, this condition is clearly a typical example.

DR. EDWARD R. MALONEY: In view of the histologic report Dr. Cannon presents with this case the diagnosis must be accepted. I certainly cannot make a clinical diagnosis of that sort. This case is one of the most interesting I have observed in a long while.

DR. GEORGE M. MACKEE: If I had seen the patient before the histologic report was given, I think I should have thought of miliary sarcoid, but I also should have thought of another possibility, which apparently is now completely out of the picture. That is miliary lipoidosis or amyloidosis.

A Case for Diagnosis (Prickle Cell Epithelioma [?] of the Glans Penis).

Presented by DR. FRED WISE.

E. S., a man aged 28, registered at the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital on Nov. 15, 1938. His disease was of five months' duration. The patient presented a lesion on the glans penis which had begun as a small painless nonindurated ulcer and apparently did not increase in depth or extent until about six weeks prior to presentation. During the past one and one-half months the ulceration has extended and is now a foul-smelling nonindurated necrotic ulcer involving three fourths of the body of the glans penis, with partial destruction of the corona and a narrow margin of the adjacent skin of the shaft. There is no pain, and the glands in the groin are not palpably enlarged. The patient's general health is unaffected. The history regarding source, time and mode of infection was too vague to be of any value. Diagnoses of syphilis, chancroid and cancer are under consideration.

Laboratory tests, with the exception of examination of biopsy material, gave negative results. The histologic structure was reported as indeterminate but "suggestive of prickle cell epithelioma." The laboratory of the health department reported infection with Vincent's organism. Three successive tests with chancroidal vaccine gave negative results.

DISCUSSION

DR. J. FRANK FRASER: The history of the case, the gross appearance of the lesion and the microscopic picture speak against the diagnosis of carcinoma. The lesion is probably chancroid.

DR. EUGENE F. TRAUB: Dr. Ludwig Loewenstein has just written an article (ARCH. DERMAT. & SYPH., to be published) on a type of fungating granuloma of the genitalia, especially the penis, which has the appearance of a malignant lesion but is actually a benign granuloma. The original article on this subject appeared in the German literature under the authorship of A. Buschke and Loewenstein (*Klin. Wchnschr.* **4**:1726 [Sept. 3] 1925). They reported a series of cases of a lesion which appeared to be unique and only on careful study could be proved nonmalignant. In view of the histologic picture in the case presented today, I should suggest that Dr. Wise get in touch with Dr. Loewenstein to see if the lesion does not belong to the group that he described.

DR. A. BENSON CANNON: If the diagnosis of carcinoma had not been suggested, I should have made one of chancroid. The youth of the patient, his having been circumcised, the rapid development and the marked destructiveness of the ulcer with the decided inflammatory reaction around the border and the soft necrotic center are all symptoms suggestive of chancroid. I believe that such a patient should be hospitalized and treatment begun immediately, with irrigations four or five times a day with 2 to 3 gallons (7.5 to 11 liters) of an antiseptic solution, followed by the application of iodoform powder. If the ulcer is chancroid, I should expect to see immediate improvement and entire healing within two or three weeks. There should, of course, be a thorough laboratory investigation of the ulcer.

DR. J. GARDNER HOPKINS: The lesion struck me as ulcerative and gangrenous balanitis in which one finds Vincent's organisms. The man gave a characteristic history of extreme phimosis with pain preceding the circumcision.

DR. EDWARD R. MALONEY: My associates and I see many lesions like this in the wards at Bellevue Hospital. They all look much alike. It struck me immediately as one of those granulomatous lesions we see so many of there. I should suggest using sulfanilamide, as we have been doing at the hospital.

DR. GEORGE M. MACKEE: I feel reasonably certain that there is no epithelioma here, histologically or clinically. Clinically, evolution has been too rapid for epithelioma. I rather think the lesion is chancroid or ulcerative phagedenic balanitis. He had, incidentally, 40 grains (2.59 Gm.) of sulfanilamide for a number of days without improvement, but he is a heavy man, and I would not be satisfied with the therapeutic test unless he had 80 or 90 or even 100 grains (5.2, 5.8 or 6.5 Gm.) a day for several days, if the drug was well tolerated.

DR. HOWARD FOX: This lesion is a destructive phagedenic ulcer, which I think is probably chancroidal in origin, although the autoinoculation test gave negative results. I saw many lesions like this in Bellevue Hospital, but they were extremely hard to cure before the advent of sulfanilamide. Previous to Louis Chargin's astonishing report of cures with this drug (ARCH. DERMAT. & SYPH. **38**:476 [Sept.] 1938) I tried it without success at Bellevue. The failure was probably due to small dosage, for later increases were followed by strikingly good results. This patient should be hospitalized and given as large doses of sulfanilamide as he can tolerate.

DR. R. H. RULISON: It seems to me that in the absence of inguinal adenitis and with the history which Dr. Hopkins has brought out, the possibility of this lesion's being chancroid is not great. As Dr. Hopkins said, I think it is a mixed infection and will probably clear under appropriate treatment.

Persistent Edema of the Eyelids, Accompanied with Rosacea and Rhinophyma. Presented by Dr. Fred Wise.

J. T., a man aged 38, Italian, registered at the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital on Feb. 8, 1938. He presented a severe grade of persistent swelling, redness and induration of the upper and lower eyelids, together with a moderate grade of rhinophyma and rosacea. The anterior surfaces of the cheeks were studded with deep pits, resembling smallpox scars, but the patient stated he had not had variola. He recalled a pustular eruption during his adolescent years.

On Nov. 8, 1937, thyroidectomy for toxic adenoma of the gland had been done at the New York Post-Graduate Medical School and Hospital. Histologic study showed "fetal adenoma with evidence of pronounced hyperactivity and regression." On Feb. 2, 1938, he was operated on for pilonidal sinus and anal fistula. During his hospitalization there appeared symptoms of an "undiagnosed form of psychosis," manifested by incoherence and outbursts of violent action. He was transferred to Bellevue Hospital, where he recovered from the mental and psychic manifestations.

When examined at the dermatologic clinic he complained only in reference to the edema of the eyelids and the rosacea. The duration of the facial eruptions was approximately one and one-half years. Physical examination, including investigation of the nasal and paranasal sinuses, revealed no abnormalities. He received a series of fourteen fractional doses (75 roentgens) of unfiltered roentgen rays, without showing any improvement. Experimental therapy with sulfanilamide proved valueless up to the day of presentation, as did a variety of local applications. He is presented for diagnosis and suggestions as to further therapy.

DISCUSSION

Dr. J. Gardner Hopkins: I think the patient has recurrent lymphangitis with lymphedema, which has resulted from an infection somewhere in the nose. The chances of its clearing without clearing of the intranasal infection first are slight.

Dr. George M. MacKee: I agree with Dr. Hopkins. This condition might be due to staphylococcus, or it might be due to streptococcus. I think a bacteriologic examination should be made. If there is a streptococcus, and there is no contraindication, sulfanilamide might be effective.

Dr. R. H. Rulison: I am puzzled by the curious punched-out follicular scarring on both cheeks, not confined to the hairy regions, which the patient said has come on gradually in the past three years. The scars originate from indolent pustules. This does not appear to me to be the ordinary scarring one sees in rosacea. I have no other diagnosis to offer, but I do not think rosacea is enough to explain the whole picture.

Dermatitis Factitia. Presented by Dr. Edward R. Maloney.

A. A., a man aged 34, presents an eruption over the lower extremities and the sides of the trunk, made up mostly of oval superficial scars. The lesions producing the scars have been appearing from time to time during the past four years. At the present time there are no active lesions other than dry crusts in two areas on the right leg, in material from which repeated attempts to find pathogenic organisms have failed. Tuberculin tests, Wassermann tests and examinations of the spinal fluid have all given negative results. There is a loss of both corneal and pharyngeal reflexes. All the lesions are in regions accessible to the patient's hands.

DISCUSSION

Dr. Paul E. Bechet: It would be interesting to know what the patient uses to produce these lesions. From the scars, it appears to be a strong acid of some sort.

(The members agreed unanimously with the diagnosis as presented.)

J. FRANK FRASER, M.D., *President*

Jan. 24, 1939

FRANK C. COMBES, M.D., *Secretary*

Extreme Maceration and Thickening of the Toe Webs (Dermatophytosis?). A Clinical Cure from the Use of "Unna's Boot." Presented by DR. HOWARD FOX.

Miss G. T., aged 28, previously presented before this society on Nov. 22, 1938 (ARCH. DERMAT. & SYPH. **39**:758 [April] 1939), has since been treated with a fixed zinc glycerogelatin dressing, and there has been a complete return to normal. A fixed dressing of this so-called Unna's boot was applied to the toes and ball of the foot on nine occasions. Each time it was left in place for five or six days. Two or three days intervened between each application, during which talcum alone was used.

DISCUSSION

DR. PAUL E. BECHET: I am particularly interested in the good results obtained by Dr. FOX because of a therapeutic suggestion offered at the previous presentation of the patient. One member suggested that electrodesiccation would be a good remedy. It struck me at the time that this was rather too radical. The good results following the simple therapeutic measures Dr. Fox took have proved my contention.

DR. A. BENSON CANNON: In my discussion of this case at the previous meeting I expressed the view that the irritation present was due to treatment rather than to a fungous disease. I suggested that an Unna's zinc glycerogelatin boot be put on the foot, thinking that by this means the parts could be immobilized and the toes separated and that the zinc glycerogelatin would probably act as a soothing, drying and protective dressing.

DR. HOWARD FOX: Whether the hypertrophic lesions were caused by fungi or bacteria I do not know. I think, however, that the basis of the trouble was hyperhidrosis. The perspiration was absorbed by the boot. The patient suffered from the condition for over two years. She was not under active treatment during all this time.

Urticaria Pigmentosa (Acquired Type). Histiocytoma Cutis. Presented by DR. EUGENE F. TRAUB.

M. E. B., a woman aged 33, presents a generalized eruption of eight years' duration. She states that the lesions appeared first on the arms, next on the chest and then on the body generally. Since the onset the eruption has never disappeared completely, although the severity varies from time to time. Several years ago, the eruption was mistaken for either parapsoriasis varioliformis or possibly ordinary parapsoriasis. At the present time, however, the eruption is typical and completely devoid of any scaling. The lesions are papular, discrete and shotty, vary in size from that of a large pinhead to that of a small pea and are dark brownish to reddish black. On friction or irritation slight wheal formation can be induced. In addition to the aforementioned eruption the patient presents a number of much larger nodules on the lower part of the back and the lower extremities. One of these when excised and examined histologically proved to be histiocytoma cutis. This result is interesting in view of the fact that some of the lesions in acquired urticaria pigmentosa are nodular, but in this case the nodular lesions are apparently not part of this disease.

Histologic examination of one of the typical lesions was reported as showing urticaria pigmentosa. Several examinations of the urine gave negative results, except that one showed 0.1 per cent sugar. The only treatment in the past has been electrodesiccation of some of the lesions on the extensor surfaces of the arms, which produced a number of deep, pitted white scars.

DISCUSSION

(The diagnosis presented was accepted unanimously by the members.)

Erythema Annulare Centrifugum (Squamous Form). Presented by DR. J. GARDNER HOPKINS.

A. H., a man aged 77, states that his eruption began in October 1924, with a "spot" on the temple. It extended that winter over the face, cleared during the summer and relapsed again in the fall of 1931, when it appeared also on the

Erythema annulare centrifugum (squamous type).

hands, arms and trunk. Since that time it has been almost continuous. The lesions occur as sharply defined circular or polycyclic plaques from 2 to 20 cm. in diameter. The borders are formed by a raised bright red ridge, which is steep at the convex border and at the concave border ends in a thick dry adherent scale. The centers of the plaques are pale pink, finely scaling and infiltrated. He has had several exacerbations on expoosure to sunlight, but the eruption is usually milder in the summer and more severe in winter. His general health has been excellent. No foci of infection have been found.

Histologic examination of one of the lesions showed decided infiltration of the lymphocytes around the blood vessels in the upper part of the cutis. The epidermis was unchanged in some areas; in others the horny layer was lifted up by large

accumulations of serum; in still others the entire epidermis was lifted up and had rubbed away, leaving the cutis exposed (this in spite of the fact that vesicles and bullae have never been visible clinically). There were an increase in the granular layer and parakeratosis.

The Wassermann reaction was negative. Examination of the blood showed no arsenic. A subcutaneous tuberculin test produced no rise in temperature. An intradermal test with staphylococcus toxin produced an extraordinary reaction, with 8 cm. of erythema and a hemorrhagic center. Tests with streptococcus toxin gave negative results.

The patient has shown some improvement recently with injections of unconcentrated liver extract.

The eruption when first seen on the face resembled lupus erythematosus. A diagnosis of erythema annulare centrifugum was later made by Dr. Sigmund Pollitzer. The picture seems to correspond morphologically with the squamous type of this eruption described by Gougerot, Merklen, Durel and other writers.

DISCUSSION

Dr. Fred Wise: I had an opportunity to see this patient four or five years ago in Dr. Pollitzer's office. At that time Dr. Pollitzer and I agreed on the diagnosis presented tonight. The lesions were far more widespread at that time, especially on the chest and abdomen. I believe it has been generally accepted that scaling is present in the disease under discussion. Previously it was thought, as Dr. Hopkins emphasized, that the epidermis was unaltered, but most of the eruptions seen and the one I described years ago under the name erythema figuratum perstans have shown similar epidermic changes. At the time of my report I was unaware of the name given to the eruption by Darier, so I gave it Wende's name, erythema figuratum perstans. There were in my case definite scaliness and sloping of the margins, and the eruption was of twenty years' duration. My patient was the brother of a physician and he died of myocarditis.

Dr. George M. MacKee: I think it is correct to accept this case as one of erythema figuratum, using this term to cover the entire group of persistent configurate erythemas. In this case a desquamative element makes it one of the squamous variety of erythema figuratum. The microscopic picture was a little unusual in one sense; the architecture was that of a vascular disease, but in the horny layer, just above the granular layer, were collections of serum. These may represent the so-called empty vesicles seen in keratolysis exfoliativa. The causation is obscure in all these cases, but the condition may be a bacterial toxemia due to a focus somewhere in the body, and it might be proper to try sulfanilamide.

Dr. Eugene F. Traub: I had 1 patient who had a dental infection. The condition apparently cleared after treatment with an autogenous vaccine and remained well for a number of years. When I saw him again, he had a fresh eruption that gradually spread over the body, casting some doubt on the value of the vaccine treatment that had been previously used. It may have been merely a coincidence that the eruption disappeared after that treatment. There is, however, no question as to the merit of the ultraviolet irradiation with the quartz mercury vapor glow lamp in the treatment of this condition. I have 2 patients now with a similar eruption, which can be made to disappear within twenty-four to forty-eight hours after a small suberythema dose of ultraviolet radiation. The result is only temporary, and new lesions continue to appear, but the effect on the lesions present at the time of exposure is truly miraculous. In 1 case I have added intramuscular injections of a bismuth preparation to the schedule of treatment and this measure has seemed to be of benefit, although it has not completely done away with the formation of new lesions. In another case, however, there have been several remissions of four to five months after a single injection of a bismuth preparation. Just why the bismuth therapy should be of benefit I do not know. In the case in which it worked so satisfactorily there was a strong reaction after the injection, and it may be that the reaction rather than the medication itself had something to do with the improvement.

DR. A. BENSON CANNON: In addition to the possibility that bacterial foci cause erythema annulare centrifugum, I wonder if one should not consider the possibility of a drug's being responsible. I saw a similar eruption in consultation a few weeks ago, and in the absence of any demonstrable foci of infection, I suggested that the patient discontinue taking the bile salts that he had been using for several years, and much to my surprise the eruption disappeared after a few days.

DR. J. GARDNER HOPKINS: I am interested in Dr. MacKee's suggestion of sulfanilamide therapy, because it has been my impression, in watching this man, that there was a similarity of these lesions to disseminated lupus erythematosus. That was my first diagnosis, but it hardly fits an eruption so extensive and at the same time so entirely benign. However, I think there is probably an etiologic relation between a number of differential dermatologic pictures, all of which are probably due to bacterial sensitization, namely, erythema multiforme, lupus erythematosus and possibly this disease too.

Granuloma Annulare with Unusual Lesions. Presented by DR. FRED WISE.

A. F., a girl aged 16, was previously presented before the Manhattan Dermatologic Society on Jan. 10, 1939 (ARCH. DERMAT. & SYPH., to be published).

DISCUSSION

DR. GEORGE M. MACKEE: Clinically the eruption suggests granuloma annulare, but the histologic picture is not what one usually expects for this disease. Histologically it is perivasculitis. The same thing is true in some cases of clinical Bazin's disease and some cases of papulonecrotic tuberculid. Whether there are two histologic types of these diseases or whether the pathologist does not happen to strike the lesion in the proper stage of evolution, I do not know, but I do not think that the histologic picture here rules out the clinical diagnosis of granuloma annulare. I accept the clinical diagnosis of granuloma annulare.

DR. FRED WISE: One of the chief factors in the clinical diagnosis of granuloma annulare is the lesion on the back of one hand which, if it had been seen alone and without regard to the history, would have been diagnosed as granuloma annulare unhesitatingly by every one. The lesions scattered over the feet detract from that diagnosis from the clinical point of view. I have little doubt that this patient has an unusual type of that disease.

DR. EUGENE F. TRAUB: What does Dr. Wise think the stippling is?

DR. FRED WISE: I want to make the same observation I made at a previous meeting, namely, that young people with granuloma annulare frequently have colorless pinhead-sized papules scattered over different parts of the body, and the histologic structure of those papules is unknown to me. I do not know whether a microscopic section of such papules would show anything even remotely resembling typical granuloma annulare. However, in this case the unusual feature is that the pinhead-sized papules exist within the discoid lesion. I think that is unusual. Tonight they were hardly visible, as a result of the roentgen treatment.

DR. GEORGE M. MACKEE: The pink waxy appearance of the nodules is seen less frequently in children than in adults. Pigmented lesions occur more frequently in children and adolescents than in adults.

Lupus Erythematosus Disseminatus. Presented by DR. EUGENE F. TRAUB.

M. S., a woman aged 53, came to the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital on Jan. 16, 1939, with an eruption of eight months' duration. The patient presents an erythematous, purpuric scaly eruption diffusely spread over the face, ears, neck and chest. There are also purpuric spots on the palms and soles. The eruption followed a sunburn.

The Wassermann and the Kahn test were negative. Examination of the urine gave negative results. A complete blood count showed 79.2 per cent hemoglobin,

3,960,000 red cells and 6,150 white cells, with 58 per cent polymorphonuclear leukocytes and 36 per cent lymphocytes. The bleeding time was five minutes; the coagulation time, nine minutes, and the reaction to a tourniquet test, negative. Histologic examination of a specimen removed for study showed acute lupus erythematosus.

DISCUSSION

DR. FRED WISE: One thing which strikes me about this case is the absence of leukopenia. On looking up the literature of acute disseminated lupus erythematosus, I got the impression that in almost 100 per cent of cases of this type there was leukopenia. I think it is rather surprising that it is absent in this case.

DR. GEORGE M. MACKEE: This type of condition should be handled cautiously, as the members all know, in relation to therapy with a gold preparation, for instance, and perhaps even with the other heavy metals. Certainly the prognosis must be at least guarded. The hemorrhagic element, the lack of margin and the diffuse spreading all indicate that this may be the type in which death occurs in a few months or a year. There have been some good reports in the literature from the use of sulfanilamide, and I have had 1 case of my own and 1 case in consultation in which clearing apparently resulted from sulfanilamide therapy.

DR. EUGENE F. TRAUB: I shall try to have this patient hospitalized for a thorough medical check-up as well as to share responsibility for the future course with an internist. The last patient presented before this society with acute disseminated lupus erythematosus was admitted to the hospital within a week after presentation and died about four weeks after admission (ARCH. DERMAT. & SYPH. **36**:1302 [Dec.] 1937).

Pigmentation of the Mouth. Bell's Palsy. Syphilis. Acne Vulgaris.
Presented by DR. HOWARD FOX.

B. H., a Negress of light color, aged 34, married, first noticed signs of paralysis of the facial nerve about five months ago. She was treated for this condition at St. Luke's Hospital, where a diagnosis of Bell's palsy of peripheral origin was made. The Wassermann reaction of the blood was then negative. At that time neither the patient nor the physician who treated her noticed any pigmentation of the tongue or other parts of the mouth. She has also been treated with roentgen rays at St. Luke's Hospital for the past five months because of acne vulgaris of the face. Her husband is now being treated for syphilis, and two months ago she was found to have a positive Wassermann reaction but gave no history of infection and presented no lesions of this disease. In the past two weeks she has received two injections of a bismuth preparation and one of neoarsphenamine. She had not previously received any antisyphilitic treatment.

Two months ago she first noticed pigmented spots on the dorsum of the tongue, palate, gums and buccal mucosa. The lesions are partly discrete and partly coalescing small macules which show no appreciable infiltration or scaling. The lesions on the tongue are dark bluish brown, and those on other parts of the mucous membrane of the mouth are yellowish brown. The burtonian line on the gums is absent. For many years the patient has taken a variety of pills and liquid medicines for constipation and for her "nerves." She does not know the nature of many of these remedies.

DISCUSSION

DR. EUGENE F. TRAUB: Some years ago I had occasion to check oral lesions in a number of Italians and other dark-skinned persons, and I found that pigmented spots like this were common on the gingival or buccal mucosa and even on the tongue. Despite the syphilitic history extending over only two months, I should be inclined to believe that these marks had been present for a longer period. This same type of pigmentation, which is seen not infrequently in Negroes and other dark-skinned persons, is found regularly in the mouths of dogs and other domestic animals.

DR. J. GARDNER HOPKINS: My impression was that those discrete round spots were unlike anything one sees from any sort of drug, and they are exactly the type of thing one sees in the mouths of Negroes. I should be inclined to agree with the previous speaker that they probably represent racial pigmentation.

DR. GEORGE M. MACKEE: I have seen pigmentation like that in several cases, both on the tongue and on the bucal mucosa and also on the lower lip. I could not determine the duration nor the cause. I finally decided they were nevoid.

DR. FRANK C. COMBES: I agree with what Dr. MacKee has said.

DR. EUGENE F. TRAUB: May I ask Dr. MacKee a question? Was that diagnosis of nevus a clinical or a microscopic diagnosis? I have taken out some of these spots, and they have showed only a little thickening, keratosis and pigmentation.

DR. GEORGE M. MACKEE: A macular pigmented nevus would show no nevus cells under the microscope—nothing but an anomaly of pigmentation.

DR. A. BENSON CANNON: While such pigmentation might be caused by a drug, I am of the belief that this discoloration is of a negroid type. The patient has the blue line on the gums that is seen so often in Negroes and, as has been remarked, the spots on the mucous membranes of the mouth and tongue are often seen in Negroes. I think, too, that the Bell's palsy is independent of the syphilitic infection.

DR. GEORGE M. MACKEE: I should like to add that in all but 1 of my patients with this condition there was no question of Negro blood. Drug eruption was excluded.

DR. GEORGE C. ANDREWS (by invitation): This pigmentation developed a month after roentgen treatment was started. I wonder if the lesions can be an unusual form of lentigenes caused by the roentgen treatment.

DR. HOWARD FOX: The patient presents a variety of lesions, including Bell's palsy, acne, syphilis and pigmentation of the mouth, but I fail to see a relation between them. She has Negro blood, though she is of light color, and I am aware that Negroes may have congenital brownish spots in the mouth. This patient, who is most intelligent, states positively that the pigmented spots have appeared within the past two months. I have confirmed this by talking with the physician at St. Luke's Hospital who treated her for Bell's palsy. In regard to Dr. Andrews' suggestion, I do not understand how a few fractional doses of roentgen rays to the skin of the face could produce pigmentation of the tongue, cheeks and palate. The patient has taken many different drugs for various ailments, but the bismuth injections at least can be eliminated as a possible cause, as they were given after the appearance of the pigmentation.

Sarcoid of Boeck (Many Atypical Lesions). Presented by DR. PAUL E. BECHET.

D. W., a Negress aged 30 states that lesions began two years ago on the face and soon thereafter spread to the arms, legs and body. She presents pigmented nevus-like growths from 1 to 2 cm. in diameter on the forehead and cheeks; on the same locations there are a dozen or so subcutaneous tumor-like growths. Fifty to a hundred or more various-sized infiltrated patches, nodules and subcutaneous tumors are scattered over the arms, legs and trunk. Some of the lesions on the legs have retrogressed, leaving definite atrophy. Others are telangiectatic in appearance.

Patch tests with old tuberculin gave negative results. Smears for acid-fast bacilli taken at the same time as the biopsy specimen were negative. A roentgen examination of the chest showed the peripheral pulmonary fields clear, with no evidence of recent parenchymatous infiltration or pleural involvement. The patient gives a history of syphilis and has a persistent 4 plus Wassermann reaction despite adequate treatment. The antisyphilitic treatment had no effect on the lesions. The histologic diagnosis from the examination of many slides confirmed the clinical diagnosis of sarcoid.

DISCUSSION

DR. FRED WISE: I should be greatly interested in knowing the histologic structure of the lesion on the forehead. It looks a good deal like lupus tumidus and also suggests leprosy.

DR. GEORGE M. MACKEE: I agree with Dr. Wise. The patient has sarcoid, but I doubt that the lesions on the forehead are sarcoid. They are grouped, coalescent nodules, soft on palpation, which is not unusual for sarcoid. They suggest lupus vulgaris. It would not be unusual to find lupus vulgaris and sarcoid in the same patient.

Erythema Figuratum Perstans. Presented by DR. FRANK C. COMBES.

C. C., a man aged 63, presents an eruption of twenty-five years' duration. The lesions fade almost entirely in the summer, a few disappearing to return again at a later date. The lesions begin as isolated papules and ultimately develop into gyrate, festooned plaques and open circles. The borders of the lesions are perceptible on palpation as a regular fine elevated ridge. In some of them there is slight scaling at the periphery. In a few the centers show slight pigmentation. There is no atrophy or scarring. There are no subjective symptoms. The patient had a penile lesion in 1904. He has had no treatment, and physical examination showed no abnormality.

The Wassermann reaction of the blood was positive. Examinations of the spinal fluid and urine gave negative results.

DISCUSSION

DR. J. GARDNER HOPKINS: I think the lesions looked like a nodular syphilid, especially the serpiginous lesions.

DR. HOWARD FOX: I cannot make a positive diagnosis of syphilis, but I think it proper to give this patient a therapeutic test in spite of his statement that the lesions have remained in the same situation for twenty-five years. He states that he had a genital sore years ago, and his Wassermann reaction is now positive.

DR. A. BENSON CANNON: I am in agreement with the view expressed by Dr. Hopkins, that this patient has serpiginous syphilis. Only the history of twenty-five years' duration would make me even consider the possibility of any other diagnosis. The serpiginous outline of the lesions with the border made up of papules and nodules (many of which are scaly) and the dark brown pigmentation in the center of the lesions (in some of which there are signs of atrophy) are most suggestive of syphilis. I should be interested not only in a study of a histologic section taken from one of the lesions but in the effects of antisyphilitic remedies on these lesions.

DR. GEORGE M. MACKEE: Histologic examination might settle the question, but tonight the discussion has to be undertaken on clinical grounds alone. There are some confusing elements. I have observed few cases of erythema figuratum that is nodular. Also there is seldom so much pigmentation. In some respects the eruption looks like a nodular serpiginous syphilid. On the other hand, the long duration is against syphilis. Other factors against syphilis are that a nodular eruption with wide distribution signifies either the late secondary or the early stage. I agree that in all probability the eruption represents an unusual example of nodular serpiginous erythema figuratum.

DR. EUGENE F. TRAUB: There is no scarring. That also is against the diagnosis of syphilis.

DR. FRANK C. COMBES: Most of the arguments against syphilis have been brought out in the discussion. I think the principal ones are the long duration of the eruption and the absence of scarring. This man is intelligent and is definite as to the duration. The genital lesion was present in 1904. No Wassermann test was done until about five years ago. While some of the lesions show distinct nodules, the majority have only a slightly elevated, even, distinct border. The appellation erythema figuratum perstans is not accurate, since some of the lesions

are papular. The patient Dr. Hopkins presented tonight also had some papular elements at the edges of the lesions, and Darier's original *érythème papulo-circiné migrateur*, with which this condition is often confused, was definitely scaly and nodular. This dermatosis, which is identical with erythema annulare centrifugum, has more distinct cordlike borders and a greater tendency to form closed lesions. I am presenting the case tonight, however, as one not of Dariers' disease but of the dermatosis described by Wende. The open circles and festooned and gyrate lesions are distinctive of this type. Another diagnosis which should be considered here is so-called tertiary erythematous syphilid (neurosyphilid of Unna) of a papular type. I know of no way to differentiate this histologically, because the picture is that of simple erythema. Of course if this patient has active syphilis, a therapeutic test would aid materially in the diagnosis.

Sarcoid of Boeck. Presented by Dr. Eugene F. Traub.

A. G., a man aged 42, came to the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital on Dec. 21, 1938, with an eruption of six months' duration. Infiltrated erythematous round or oval lesions of different sizes are scattered over the back, the external aspect of the right arm and the anterior portion of the right ear.

The Wassermann and the Kahn test were negative. Urinalysis gave negative results. Histologic examination of a biopsy specimen taken from the middle of the back showed sarcoid of Boeck, and that of a second specimen confirmed the report on the first. Roentgenograms of the chest showed a moderate degree of old lymphoid nodulation at the hilus, with secondary root branch and central bronchial thickening. The productive changes were perhaps a shade more discernible on the right side, where slight interlobar septal thickening also existed. These changes appeared to be of long standing, with no definite evidence of recent parenchymatous infiltration or pleural involvement. The diagnosis was chronic hilar, root branch and central bronchial thickening. Roentgenograms of the hands and the forearms were normal. Smears showed no lepra bacilli. Tuberculin tests showed the following results: On the left arm, the reaction to old tuberculin was indefinite with dilutions of 1 : 5,000 to 1 : 1,000 and 1 plus with a dilution of 1 : 500; with all dilutions of special tuberculin I and special tuberculin II it was negative. On the right arm old tuberculin produced a 1 plus reaction with a dilution of 1 : 100 and showed 2.3 cm. of infiltration and 2.6 cm. of erythema with a dilution of 1 : 10; special tuberculin I and special tuberculin II produced negative reactions with dilutions of 1 : 100 and 1 : 10.

DISCUSSION

Dr. George M. MacKee: Histologically there are sharply defined nodules, a few giant cells and a fairly definite tuberculoid structure. I think the condition is sarcoid both clinically and histologically, but taking the histologic picture alone I think that leprosy would have to be considered, because one occasionally encounters a histologic architecture like this in leprosy.

Dr. Eugene F. Traub: Two specimens were removed for examination. Some of the physicians who looked at the first slide thought there might be a question of leprosy, and for this reason a second specimen was removed. Dr. Satenstein thought both slides showed an appearance typical of sarcoid. I cannot say which of the two sections was sent over for examination this afternoon. It may have been one of the first slides, which did not in all instances show a large portion of the typical lesion.

Dr. J. Frank Fraser: The histologic evidence was in favor of a diagnosis of sarcoid. There was tubercle formation, and the tubercles were separated from each other by bands of fibrous tissue. In some respects, at first glance, the extreme vacuolation of the cells would suggest leprosy, but the infiltration was not diffuse, as in the cases of leprosy I have observed. The giant cells were of the type one

sees in sarcoid. They had, for example, the foamy cytoplasm which is generally regarded as characteristic. I favor the diagnosis of sarcoid on both histologic and clinical grounds.

DR. HOWARD FOX: Both the clinical appearance of the lesion and tuberculoid structure (histologically) would be compatible with a diagnosis of leprosy. There are, however, no other signs or symptoms of this disease. I favor the diagnosis of sarcoid.

DR. FRED WISE: I understood that the sarcoid lesions in the leper are indistinguishable from the sarcoid lesions in the tuberculous patient. There are no distinctive lepra cells in the sarcoid of a leper. I believe the condition was described by Jadassohn as sarcoid in a leper without microscopic evidence of leprosy in the biopsy specimen.

DR. EUGENE F. TRAUB: I saw no evidence to substantiate the diagnosis of leprosy. Smears were obtained after the administration of potassium iodide, and these gave negative results.

Book Reviews

Corpus Iconum Morborum Cutaneorum. Edited by Dr. Louis Nékám (Budapest, Hungary). Volume V, Parts 1-3. Cloth, 194 marks. Pp. 180; 464; 928, with illustrations. Leipzig: Johann Ambrosius Barth, 1938.

This atlas of cutaneous diseases forms volume 5 of the transactions of the Ninth International Congress of Dermatology and Syphilology, held at Budapest, Hungary, in 1935. It consists of three separately bound books. The second and third contain 4,566 illustrations, including photomicrographs contributed by 568 dermatologists from all over the world. Following the recommendation of the committee on classification, the diseases are classified according to combined morphologic-etiologic criteria. They are divided into the following eight groups, each of which has subdivisions: (1) changes due to living causes; (2) changes due to external causes; (3) changes due to internal causes; (4) changes probably autochthonous, often of uncertain causation; (5) tumors; (6) hereditary changes; (7) changes due to abnormal evolution, and (8) functional and structural changes. The names of the diseases are designated in Latin. Syphilis is illustrated on 55 pages; comparative dermatology takes up 19 pages, and on 60 pages the illustrations are colored. As this volume is the first of a series, some photographs were used which had been published by early masters of dermatology, including Vidal, Fournier, Besnier, Hallopeau and others. The first part contains 180 pages of explanations of the illustrations. Because of the cost, the explanations are given in abbreviated telegraphic style, and words which are frequently used are designated by hieroglyphic signs. The text is written in English, French, German and Italian, according to the nationality of the contributor, and because of the difficulty of many dermatologists in reading foreign languages in abbreviated style, Greek and Latin terms are used as much as possible. These abbreviations in dead and in living languages and the hieroglyphic signs are explained in a special table. The text does not give detailed descriptions of the cases, as this material is supplementary to the illustrations.

Dr. Nékám deserves much praise for this rich collection of illustrations representing up-to-date dermatology. The reviewer, however, permits himself to criticize a few features, with the hope that such criticism may enhance the value of the next atlas. A fair number of photographs could have been eliminated, some because of repetition and others because of poor photography. Of greater importance, however, is the fact that the responsibility for the diagnosis has been left entirely to the contributor. As an example I wish to call attention to illustration 412, which shows, according to the diagnosis of Dr. K. Buday, syphilitic stricture of the rectum. The text does not explain how such a diagnosis was made. Since it has been found that most rectal strictures are due to the virus of lymphogranuloma venereum, although previously thought to be syphilitic, it is a priori doubtful if rectal stricture due to syphilis exists at all. The contributor is obliged to prove in such a case the diagnosis he offers. I believe, therefore, that only such diagnoses should be accepted as have been proved to the satisfaction of a committee of outstanding members of the congress.

In spite of this criticism, this atlas must be considered an outstanding contribution to the dermatologic literature. The idea of Dr. Nékám of continuing to publish such collections should be enthusiastically received, as it would show the dermatologist the progress of his specialty by means of illustrations.

Directory of Dermatologic Societies *

INTERNATIONAL

TENTH INTERNATIONAL CONGRESS OF DERMATOLOGY AND SYPHILOLOGY
Oliver S. Ormsby, President, 25 E. Washington St., Chicago.
Paul A. O'Leary, Secretary-General, 102–2d Ave. S. W., Rochester, Minn.
Place: New York. Time: Summer 1940.

PAN AMERICAN MEDICAL ASSOCIATION, SECTION OF DERMATOLOGY AND SYPHILOLOGY
Elmore B. Tauber, President, 19 W. 7th St., Cincinnati.
Austin W. Cheever, Secretary, 49 Bay State Rd., Boston.

FOREIGN

BRITISH ASSOCIATION OF DERMATOLOGY AND SYPHILOLOGY (CANADIAN BRANCH)
Harold Orr, President, 10189–101st St., Edmonton.
Don Mitchell, Secretary-Treasurer, 1414 Drummond St., Montreal.

ROYAL SOCIETY OF MEDICINE, SECTION OF DERMATOLOGY
H. W. Barber, President, 7 Devonshire Pl., London, W. 1, England.
Louis Forman, Secretary, 7 Devonshire Pl., London, W. 1, England.

NATIONAL

AMERICAN MEDICAL ASSOCIATION, SCIENTIFIC ASSEMBLY, SECTION ON DERMATOLOGY AND SYPHILOLOGY
John G. Downing, Chairman, 520 Commonwealth Ave., Boston.
C. F. Lehmann, Secretary, 705 E. Houston St., San Antonio, Texas.
Place: New York: Time: June 10-14, 1940.

AMERICAN ACADEMY OF DERMATOLOGY AND SYPHILOLOGY
Paul A. O'Leary, President, Mayo Clinic, Rochester, Minn.
Earl D. Osborne, Secretary, 471 Delaware Ave., Buffalo, N. Y.
Place: Philadelphia.

AMERICAN BOARD OF DERMATOLOGY AND SYPHILOLOGY
Howard Fox, President, 140 E. 54th St., New York.
C. Guy Lane, Secretary-Treasurer, 416 Marlborough St., Boston.

AMERICAN DERMATOLOGICAL ASSOCIATION
Francis E. Senear, President, 55 E. Washington St., Chicago.
Fred D. Weidman, Secretary, University of Pennsylvania, Philadelphia.

SOCIETY FOR INVESTIGATIVE DERMATOLOGY
Joseph V. Klauder, President, 1934 Spruce St., Philadelphia.
S. W. Becker, Secretary, University of Chicago, Department of Medicine, Chicago.

* Secretaries of dermatologic societies are requested to furnish the information necessary for the editor to make this list complete and to keep it up to date.

SECTIONAL

Central States Dermatological Association

John C. Kerr, President, 621–14th St., Wheeling, W. Va.
Marvin B. Goldstein, Secretary-Treasurer, Stambaugh Bldg., Youngstown, Ohio.
Place: Buffalo, N. Y. Time: Spring 1940.

Mississippi Valley Dermatological Society

Hamilton Montgomery, President, Mayo Clinic, Rochester, Minn.
Herbert Rattner, Secretary-Treasurer, 25 E. Washington St., Chicago.
Place: Chicago.

New England Dermatological Society

Fred S. Burns, President, 83 Marlborough St., Boston.
B. Appel, Secretary, 483 Beacon St., Boston.

Northern New Jersey Dermatological Society

Louis J. B. Le Bel, President, 165 Grant Ave., Nutley.
C. C. Carpenter, Secretary, 38 Waldron Ave., Summit.
Place: Academy of Medicine of Northern New Jersey, Newark. Time: Third Tuesday of March, April, October and December.

Southeastern Dermatological Association

J. R. Allison, Chairman, 1121 Barnwell St., Columbia, S. C.
Howard King, Secretary, 328 Doctors Bldg., Nashville, Tenn.
Place: Vanderbilt Hospital, Nashville, Tenn. Time: Sept. 3, 1939.

Southern Medical Association, Section on Dermatology and Syphilology

J. Richard Allison, Chairman, 1512 Marion St., Columbia, S. C.
Clinton W. Lane, Secretary, 508 N. Grand Ave., St. Louis.

STATE

California Medical Association, Scientific Assembly, Dermatology and Syphilology Section

Norman N. Epstein, Chairman, 450 Sutter St., San Francisco.
Arne E. Ingels, Secretary, 490 Post St., San Francisco.

Connecticut State Medical Society, Section on Dermatology

James D. Gold, Chairman, 839 Myrtle Ave., Bridgeport.
Albert Levenson, Secretary, 881 Lafayette St., Bridgeport.

Florida Society of Dermatology and Syphilology

Elmo D. French, Chairman, Huntington Bldg., Miami.
Lauren M. Sompayrac, Secretary, 459 St. James Bldg., Jacksonville.

Louisiana Dermatological Society

M. T. Van Studdiford, President, 912 Pere Marquette Bldg., New Orleans.
R. A. Oriol, Secretary-Treasurer, 921 Canal St., New Orleans.

Massachusetts Medical Society, Section on Dermatology and Syphilology

E. Lawrence Oliver, President, 20 Fairfield St., Boston.
J. G. Downing, Secretary, 520 Commonwealth Ave., Boston.

Medical Society of the State of New York, Section on Dermatology and Syphilology

Frank C. Combes, Chairman, 80 W. 40th St., New York.
Rudolph Ruedemann Jr., Secretary, 256 State St., Albany.

MEDICAL SOCIETY OF THE STATE OF PENNSYLVANIA
SECTION ON DERMATOLOGY

William D. Whitehead, Chairman, Medical Arts Bldg., Scranton.
V. C. Garner, Secretary, Germantown Professional Bldg., Philadelphia.

MICHIGAN STATE MEDICAL SOCIETY, SECTION ON DERMATOLOGY AND SYPHILOLOGY

Ruth Herrick, Chairman, 26 Sheldon Ave. S. E., Grand Rapids.
Eugene A. Hand, Secretary, 801 Second National Bank Bldg., Saginaw.

MINNESOTA DERMATOLOGICAL SOCIETY

E. M. Rusten, President, 78 S. 9th St., Minneapolis.
F. W. Lynch, Secretary-Treasurer, Lowry Medical Arts Bldg., St. Paul.
Time: First Friday in October, December, February and April.

OKLAHOMA STATE DERMATOLOGICAL SOCIETY

M. M. Wickham, President, Norman.
W. A. Showman, Secretary, 108 W. 6th St., Tulsa.

TEXAS DERMATOLOGICAL SOCIETY

Leslie Smith, President, 109 N. Oregon St., El Paso.
Duncan O. Poth, Secretary, 414 Navarro St., San Antonio.

LOCAL

BALTIMORE-WASHINGTON DERMATOLOGICAL SOCIETY

Francis A. Ellis, President, 104 W. Madison St., Baltimore.
I. Louis Sandler, Secretary, 1835 I St. N. W., Washington, D. C.
Place: Alternate cities. Time: Third Thursday of each month.

BRONX DERMATOLOGICAL SOCIETY

Marion B. Sulzberger, President, 962 Park Ave., New York.
Henry Silver, Secretary, 290 West End Ave., New York.

BROOKLYN DERMATOLOGICAL SOCIETY

M. J. Cantor, President, 907 St. Marks Ave., Brooklyn.
S. H. Silvers, Secretary, 920 Bushwick Ave., Brooklyn.
Time: Third Monday of each month except June, July, August and September.

BUFFALO-ROCHESTER DERMATOLOGICAL SOCIETY

Richard L. Saunders, President, 333 Linwood Ave., Buffalo.
James W. Jordon, Secretary, 471 Delaware Ave., Buffalo.

CENTRAL NEW YORK DERMATOLOGICAL SOCIETY

Harry D. Parkhurst, President, 264 Genesee St., Utica.
Maxwell C. Snider, Secretary, 106 Oak St., Binghamton.

CHICAGO DERMATOLOGICAL SOCIETY

Edward A. Oliver, President, 55 E. Washington St., Chicago.
Herbert Rattner, Secretary, 25 E. Washington St., Chicago.

CINCINNATI DERMATOLOGICAL SOCIETY

Daniel J. Kindel, President, 1910 Union Central Bldg., Cincinnati.
Lawrence Goldberg, Secretary-Treasurer, Doctors Bldg., Cincinnati.
Place: Cincinnati. Time: First Wednesday of each month, except June, July, August and September.

Cleveland Dermatological Society

John Gammel, President, 1020 Huron Rd., Cleveland.
Charles G. La Rocco, Secretary, 2060 E. 9th St., Cleveland.

Detroit Dermatological Society

A. R. Woodburne, President, 612 Medical Arts Bldg., Grand Rapids, Mich.
Ruth Herrick, Secretary-Treasurer, 528 Medical Arts Bldg., Grand Rapids, Mich.

Kansas City (Mo.) Dermatological Society

C. C. Dennie, President, 1103 Grand Ave., Kansas City.
Thomas B. Hall, Secretary, 902 Professional Bldg., Kansas City.

Los Angeles Dermatological Society

Thomas W. Nisbet, President, 65 N. Madison Ave., Pasadena, Calif.
C. R. Caskey, Secretary, 1930 Wilshire Blvd., Los Angeles.
Time: Second Tuesday of each month, October to May, inclusive.

Manhattan Dermatologic Society

George C. Andrews, Chairman, 115 E. 61st St., New York.
Anthony C. Cipollaro, Secretary, 40 E. 61st St., New York.

Montreal Dermatological Society

L. P. Ereaux, President, 1390 Sherbrooke St. W., Montreal, Canada.
Paul Poirier, Secretary, 456 Sherbrooke St. E., Montreal, Canada.

New York Academy of Medicine, Section of Dermatology and Syphilis

Eugene F. Traub, Chairman, 140 E. 54th St., New York.
Louis Tulipan, Secretary, 224 E. 17th St., New York.

New York Dermatological Society

Frank C. Combes, President, 80 W. 40th St., New York.
J. Gardner Hopkins, Secretary-Treasurer, 102 E. 78th St., New York.

Omaha Dermatological Society

Donald J. Wilson, President, 1113 Medical Arts Bldg., Omaha.
Leonard J. Owen, Secretary-Treasurer, 954 Stuart Bldg., Lincoln, Neb.

Philadelphia Dermatological Society

Thomas Butterworth, Chairman, 411 Walnut St., Reading, Pa.
Herman Beerman, Secretary, 255 S. 17th St., Philadelphia.
Time: Third Friday of each month from September to May, inclusive.

Pittsburgh Dermatological Society

John C. Kerr, President, 62–14th St., Wheeling, W. Va.
Marvin B. Goldstein, Secretary, Stambaugh Bldg., Youngstown, Ohio.
Time: Third Thursday of every month except July and August.

St. Louis Dermatological Society

Martin F. Engman Jr., President, 3720 Washington Blvd., St. Louis.
Roy L. Kile, Secretary-Treasurer, 3720 Washington Blvd., St. Louis.
Place: Barnard Free Skin and Cancer Hospital. Time: 2 p. m., second Wednesday of each month.

San Francisco Dermatological Society

Merlin T.-R. Maynard, President, San Jose, Calif.
H. V. Allington, Secretary, 3115 Webster St., Oakland, Calif.
Time: Third Friday of February, April, September and November.